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PURPURIC PIGMENTED LICHENOID DERMATITIS

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Purpuric pigmented lichenoid dermatitis was the title which Gougerot and Blum gave to a cutaneous condition which they observed occurring with rare frequency but having characteristics which convinced them that they were assigning a name to an entity which had not been previously described or recorded in the dermatologic literature.

The disease was defined as a widely disseminated superficial dermatosis of insidious onset and chronic course, producing only trivial subjective symptoms and morphologically characterized by minute rust-colored papules often collected into plaques with poorly marked boundaries. Except for its distribution, the condition had the general appearance of Schamberg's progressive pigmentary dermatosis. The underlying cause, although unknown, pointed to a capillaritis with extravasation or diapedesis of red blood corpuscles. Since the publication of the report by Gougerot and Blum, enough other cases have been recognized to warrant the recording of our observations and investigations on patients with an eruption the diagnosis of which was pigmented purpuric lichenoid dermatitis.

REVIEW OF THE LITERATURE

As is always the case with a newly recognized dermatosis, the literature is confined to the essays of the original authors.

In 1925, Gougerot and Blum [1] presented to the French Dermatological Society a man 41 years of age who complained of an itchy eruption on the legs of fifteen months' duration. The lesions, which were symmetrically placed on the medial surface of the middle and lower portions of the extremities, consisted of ocher-colored pigmented plaques, which on closer inspection were found to be made up of tiny, brilliant, slightly raised papules. Sharply demarcated purpuric points and large violaceous ecchymotic areas were also seen along with the other lesions. The rest of the body, including the mucosae, was free from purpura, papules or pigmented plaques, and the general physical

From the Division of Dermatology, University of Minnesota, Dr. Henry E. Michelson, director.

1. Gougerot, H., and Blum, Paul: Purpura angioscléreux prurigineux avec éléments lichénoïdes, Bull. Soc. franç. de dermat. et syph. **32**:161, 1925.

examination showed no underlying abnormalities. Civatte, in commenting on the histologic characteristics of the condition, stated that there were granules of iron pigment present beneath a thinned epidermis and a slight sclerosis of the cutis. Although lichen planus, eczema and prurigo were considered as diagnostic possibilities, Gougerot and Blum called the eruption "purpura angioscléreux prurigineux avec éléments lichénoïdes."

The second case was seen by them [2] shortly afterward. In this case the eruption was present on the left arm and left leg. The patient, a woman aged 31, stated that the oldest lesion, which was a round, pigmented plaque on the upper portion of the left forearm, had been noticed for about eleven years. An identical lesion was observed in the middle of the forearm in addition to irregular plaques of bizarre aspect on

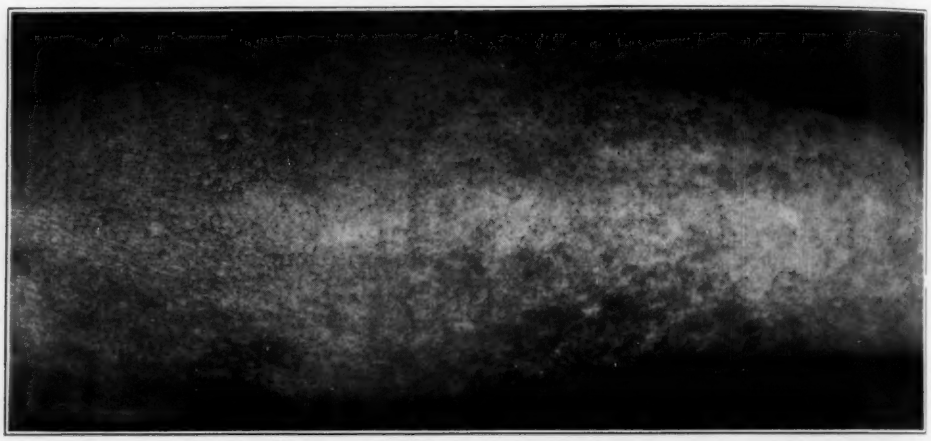

Fig. 1 (case 1).—Purpuric pigmented lichenoid dermatitis of ten years' duration on the skin of a man (S. O.) aged 45. The condition occurred in attacks and consisted of minute papules on the legs and lower portion of the trunk. The development of generalized erythroderma was followed by recovery and recurrence of the papular eruption.

the anteromedial and posteromedial surfaces of the left thigh. Brown pigmentation, redness not disappearing on diascopic pressure and telangiectasia were the salient features of the plaques. In the region of the internal and external malleoli of the left ankle there was a melange of lichenoid lesions and purpuric spots. Here the brilliant tiny papules so prominent in the first case could be clearly distinguished. Similar efflorescences were present on the dorsal surface of the great toe. The mucous membranes were free; the general health was good, and the lesions were asymptomatic.

2. Gougerot, H., and Blum, Paul: Un 2e cas de dermatite lichénoïde purpurique et pigmentée, Bull. Soc. franç. de dermat. et syph. **32**:433, 1925.

Darier, on seeing this patient, brought the diagnosis of Schamberg's disease into consideration.

Gougerot, having had his curiosity aroused by this new kind of rash, found a similar eruption in a 43 year old man, whom he and Faton [3] presented to the French Dermatological Society in March 1926. The patient was vigorous and had no apparent visceral disease, though the bleeding and clotting times were prolonged. The eruption, though similar in its general features to the previously observed examples, was broader in its distribution, involving the arms, flanks, sacral region and thighs. The lesions were smaller but more numerous and showed less confluence and pigmentation than in the other cases. On the legs the characteristic papules were most numerous and purpuric. The same indolent, asymptomatic course was noticed. The eruption involuted slowly without atrophy and within a year was almost healed. By December 1928 the lesions had entirely disappeared.

Gougerot and Blum recorded their findings after seeing a fourth [4] example of this rare dermatosis, and from experience and knowledge gained in examining and observing their previous cases they reported the details concerning purpuric pigmented lichenoid dermatitis. Later a fifth [5] case was observed.

Since that time no formal articles have been published. However, attention having been attracted to the unique and euphonious title, Wise,[6] Ormsby [7] and one of us (H. E. M.[8]) ventured this diagnosis on cases presented before the Chicago Dermatological Society and the American Dermatological Association. Dr. O. J. Cameron, of Omaha, showed us photographs of a patient with an eruption which apparently belongs to this group. Thus it is evident that dermatologists are on the alert for this rare but quite characteristic condition, and undoubtedly many examples will be discovered in due course of time.

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3. Gougerot, H., and Faton: Dermatite lichénoïde et purpurique innominée, Bull. Soc. franç. de dermat. et syph. **33**:188, 1926.

4. Gougerot, H., and Blum, Paul: Dermatite lichénoïde purpurique et pigmentée. Comparison avec la maladie de Schamberg, Arch. dermat.-syphiligr. **1**:555, 1929.

5. Gougerot, H., and Blum, Paul: Nouveau cas de dermatite lichénoïde purpurique et pigmentaire, Bull. Soc. franç. de dermat. et syph. **6**:889, 1934.

6. Wise, Fred: A Case for Diagnosis (Dermatite lichénoïde purpurique et pigmentée of Gougerot and Blum or Schamberg's Progressive Pigmentary Dermatosis?), Arch. Dermat. & Syph. **30**:873 (Dec.) 1934.

7. Ormsby, Oliver S.: Diseases of the Skin, Philadelphia, Lea & Febiger, 1934, p. 216.

8. Michelson, H. E., in discussion on Ziesler, E. P.: Schamberg's Progressive Pigmentary Dermatitis (?), Arch. Dermat. & Syph. **28**:255 (Aug.) 1933; in discussion on Senear, F. E., and Caro, Marcus R.: A Case for Diagnosis (Schamberg's Disease?), ibid. **28**:734 (Nov.) 1933.

CLINICAL FEATURES OF PURPURIC PIGMENTED LICHENOID DERMATITIS

Correlation of the descriptions and views of purpuric pigmented lichenoid dermatitis must be made from the written descriptions and photographs. They may be misconstrued, and the danger of exploiting the name without rigid adherence to the definition of Gougerot and Blum must be avoided.

The clinical features of purpuric pigmented lichenoid dermatitis as exhibited by the various cases recorded to date have been almost uniform, varying only in some of the minute details.

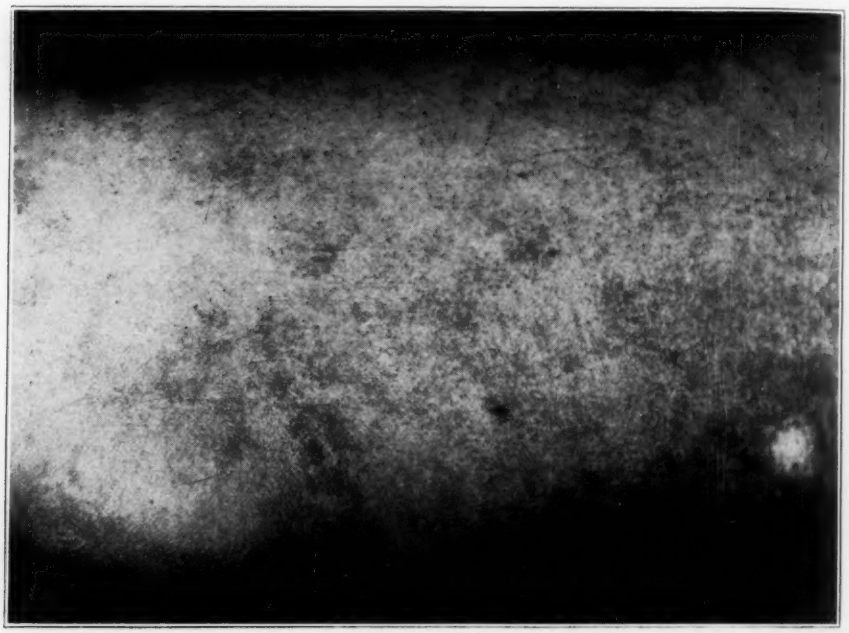

Fig. 2 (case 2).—Purpuric pigmented lichenoid dermatitis of one year's duration on the skin of a woman (E. J.) aged 36. The condition began on the ankles and gradually spread to the legs, thighs, abdomen and upper parts of the arms. Although the bleeding and clotting times were normal, tests of the fragility of the erythrocytes (tourniquet and pinching) gave positive results.

The age and sex of the patients play no important part in the onset of the disease, as evidenced by the extreme variations in age and in the lack of confinement to one sex. In all instances the condition begins without a definite date of onset, making its appearance insidiously, and the lesions gradually become more numerous. There are usually no accompanying subjective symptoms, although some of the patients complain of itching.

The initial lesion of purpuric pigmented lichenoid dermatitis is a tiny smooth, slightly elevated round papule of brilliant red or orange.

The diameter is from 0.25 to 2. mm. Occasionally the outline is irregular, even angular, and it therefore resembles a papule of lichen planus. Since the lesion is somewhat dependent on an extravasation of blood, there is a change in color, which depends on the age of the lesion. Early papules are the color of fresh arterial blood, which later changes to the darker hue of purpura. The final and more permanent shade is a sepia brown. Papules of all ages may be present in a small area. In fact, there is a tendency toward formation of plaques, with papules densely packed in the center, more scattered at the periphery and then gradually fading out into the surrounding normal skin.

Purpuric pigmented lichenoid dermatitis occurs more commonly on the legs, thighs and lower portion of the trunk. The chest and head are spared, but lesions may occur on the arms. On the parts in which lesions are the most common, plaques are more likely to form, while in the less commonly invaded areas isolated papules are to be found. The individual papules are identical with the single lesions found in Schamberg's disease.

In one of our cases an eruption became almost universal and finally arrived at a state which resembled acute generalized erythroderma. Exfoliation took place, and later a return of rather typical papules was observed. In the other cases observed or recorded the course was not severe and there was no exfoliation. Exudation with crusting or scaling has not been mentioned except as already recorded.

As the disease becomes older, telangiectatic and purpuric papules, especially on the lower extremities, after appearing, become quite stationary, giving the appearance of embedded grains of paprika.

The vital organs of the patients are not affected, and aside from the man who had exfoliative dermatitis (this may have been due to self-medication) and one patient observed by Gougerot and Blum, who had signs of a purpuric diathesis, the course has been practically asymptomatic. Except for the appearance of the lesions, the patients were unaware of the presence of the eruption.

HISTOLOGIC CHARACTERISTICS

The histologic picture of purpuric pigmented lichenoid dermatitis is not pathognomonic, and the characteristics are not fixed. The borders of the papules can be fairly well determined microscopically. Any epidermal change is entirely secondary, consisting of thinning or an insignificant degree of hyperkeratotic or parakeratotic scaling. The principal changes occur in the papillary portion of the cutis; they consist of edema, resulting in a certain spreading apart of the collagen bundles, and a sparse, nonspecific infiltration of lymphocytes and free red blood corpuscles. The lesion as a whole microscopically resembles

a well developed papule of lichen nitidus in its general outline, the difference being in the cells of the infiltrate, especially the presence of red blood corpuscles. Gougerot and Blum emphasized the finding of minute blood vessels in the cutis, particularly swollen ectatic capillaries, some of which showed endothelial proliferation even to the point of obliteration of the lumens. They believed that this capillaritis played an important part in the pathogenesis. The altered capillaries served as an axis for the zone of infiltrate, which was made up of lymphocytes,

Fig. 3 (case 3).—Purpuric pigmented lichenoid dermatitis present for four months on the skin of a woman (Mrs. E. N.) aged 51. It began with tiny papules on the ankles which formed plaques and spread up the leg to the knee. The general health was good.

fibroblasts, red blood corpuscles and a few plasma cells. There were no areas of hemorrhage, and the normal appearance of the red blood corpuscles enmeshed in the zone gave the impression that they had arrived by diapedesis rather than through rents in the vessels.

The connective tissue is affected secondarily, but it has no important part in the process. Granules of iron pigment may or may not be present.

DIAGNOSIS

The differentiation of purpuric pigmented lichenoid dermatitis from Schamberg's progressive pigmentary disorder presents the chief problem in diagnosis. Other closely related purpuric pigmentary syndromes, such as purpura annularis telangiectodes, angioma serpiginosum and a type of purpuric parapsoriasis recently described by Gougerot and Blum, must also be considered. Lichen planus, the tuberculids, eczema and prurigo were also mentioned in connection with the cases of Gougerot and Blum. The resemblance to any of these disorders is only superficial and less apparent after careful observation. Lichen planus is easily excluded.

The chief difference between purpuric pigmented lichenoid dermatitis and Schamberg's disease is in the distribution of the lesions. Gougerot and Blum emphasized the papular character of purpuric pigmented lichenoid dermatitis, but in dealing with such tiny lesions it is very difficult to determine the difference between a minute papule and a puncta. For our own part, we believe that if our interpretation of the cases which we have diagnosed as instances of purpuric pigmented lichenoid dermatitis is correct and the cases therefore can be identified with those of Gougerot and Blum, the individual small components cannot be distinguished from those of Schamberg's disease, and hence the extent of the eruption will be the deciding factor. This same thought must have occurred to the other American observers, because the cases were presented as examples of generalized Schamberg's disease before the authors had heard of the decision of Gougerot and Blum to name a dermatosis resembling Schamberg's disease, but more papular and wider in its scope, purpuric pigmented lichenoid dermatitis. In our opinion, Schamberg's disease, being confined to the lower extremities and having been described before the newer work on varicosities, might well be associated with or directly caused by invisible or deeply lying altered veins. Then, too, certain of the conditions placed in the livedo group bring about extravasations and vascular changes. Some such conditions might be the underlying cause of Schamberg's disease in young persons, while invisible varicosities could bring about the change in older patients. We have repeatedly examined persons with varicose veins who have had stasis dermatoses identical clinically with what is commonly called Schamberg's disease, and since we have been on the lookout for this condition we have seen patients of both sexes with about the same frequency having patches of progressive pigmentary dermatitis about varicosities. In cases of purpuric pigmented lichenoid dermatitis the fragility of the blood vessels with the subsequent change must be effected through some other element; hence the broader distribution. Morphologically, Schamberg's disease will stand as a condition consisting of plaques of varying size, on the lower part of the

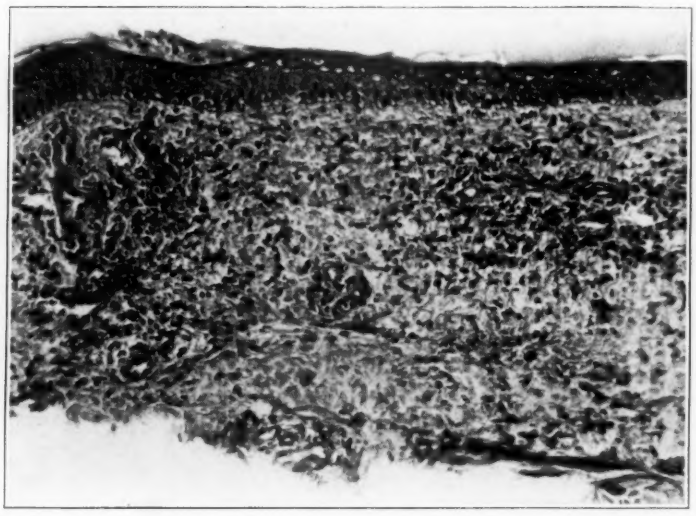

Fig. 4.—Photomicrograph illustrating the picture usually seen in purpuric pigmented lichenoid dermatitis. Note especially the capillaritis and the infiltrate.

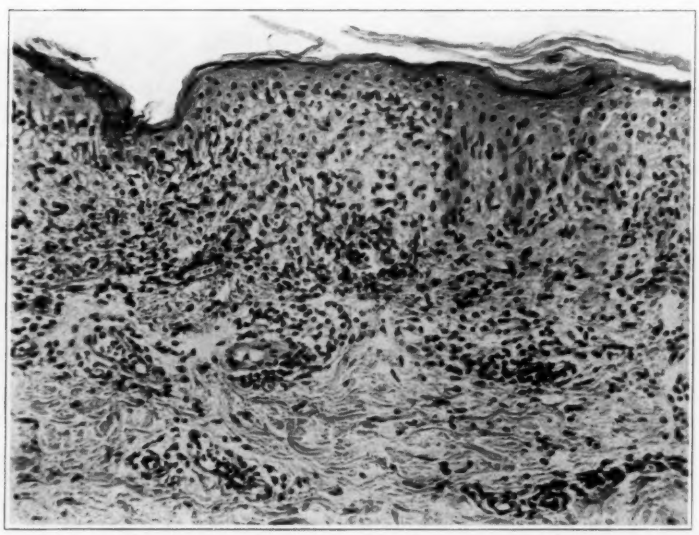

Fig. 5 (case 1).—Photomicrograph of a lesion from the abdomen showing the same characteristics seen in figure 4. Note especially the blood vessels and the free red blood corpuscles.

leg, made up of minute puncta the color of cayenne pepper, which with time change in color from red to brown and remain as permanent brown stains. On section, deposits of hemosiderin are found. Kingery,[9] evidently after a careful study of a case, concluded that in Schamberg's disease there was a primary circulatory disturbance. Templeton [10] made a careful differentiation between Schamberg's, Majocchi's and Hutchinson's disease. He expressed the belief that Schamberg's disease is a chronic process, characterized by patches of pigmentation which spread peripherally by new satellite puncta and lack annular lesions and purpura. He emphasized its predominance in persons of the male sex.

Purpura annularis telangiectodes is characterized by small and at times depressed red telangiectatic macules which soon become purpuric and even necrotic, healing with an atrophic scar. About the scar there is often a residual pigmentation. The condition occurs most commonly about the ankle, and the process tends to be self-healing. In our opinion, this disease is a form of purpura, severe enough locally to cause necrosis but not markedly disturbing the general economy, most patients remaining ambulant. The residual pigmented plaques somewhat resemble Schamberg's disease, but the difference is noted at first sight. On healing, certain small varicose ulcers resulting from stellate varicosities look almost identical with the lesions in Majocchi's disease, the course and distribution alone serving as differential points. Majocchi's disease does not look at all like purpuric pigmented lichenoid dermatitis.

The question of the clinical picture of angioma serpiginosum cannot be regarded as definitely settled, and the condition has been confused with other dermatoses, such as Majocchi's disease and telangiectatic lupus erythematosus. Wertheim [11] regarded angioma serpiginosum as a peculiar form of angioma which grows slowly and involutes in the center while it spreads peripherally, so that in the course of years circinate plaques with elevated borders and sunken, slightly atrophic centers are formed. In the surrounding skin are grouped satellite angiomas, which also finally undergo the same development. True angioma serpiginosum is extremely rare, and the case of Wise and Pollitzer [12] seems to be a classic example. We have found no other authentic examples and are unable to discuss angioma serpiginosum in

9. Kingery, Lyle B.: Schamberg's Progressive Pigmentary Dermatosis, J. Cutan. Dis. **36**:166, 1918.

10. Templeton, H. J.: Progressive Pigmentary Dermatosis (Schamberg), Arch. Dermat. & Syph. **16**:141 (Aug.) 1927.

11. Wertheim, Leo: Haemangiome (einschliesslich der Telangiektasien und verwandter Hautveränderungen), in Jadassohn, J.: Handbuch der Haut.- und Geschlechtskrankheiten, Berlin, Julius Springer, 1932, vol. 12, pp. 377 and 405.

12. Wise, Fred, and Pollitzer, S.: Angioma Serpiginosum (Infective Angioma of Hutchinson), with Report of a Very Extensive Case, J. Cutan. Dis. **31**:725, 1913.

relation to purpuric pigmented lichenoid dermatitis more than to say that Hutchinson's disease seems definitely nevoid in the sense of an angioblastoma. One of our cases described by Madden as an instance of telangiectatic nevus seemed to us to be closely related to this syndrome.

Gougerot and Blum [13] recently observed a man 35 years of age who presented peculiar lesions on the shoulders, trunk and flanks. These lesions consisted of raised, shiny papules from 0.25 to 2 mm. in diameter and plaques from 2 to 6 cm. broad which were surrounded by the small

Fig. 6 (case 2).—View (high power field) of a lesion from the arm of a woman (E. J.), showing the details of the infiltrate and new vessels.

isolated papules. The lesions were further characterized by dilated and ruptured capillaries, which gave rise to tiny purpuric points and later to violaceous brown pigmentation. The disease was of slow evolution and of two years' duration. Examination showed that the bleeding and clotting times were abnormal. Histologic sections were made, and an inflammatory process in the cutis was found, consisting of edema, formation of new blood vessels, lymphocytic infiltration, extravasation of

13. Gougerot, H., and Blum, Paul: Parapsoriasis ponctué et en plaques, télangiectasique, purpurique et pigmentaire (forme avec capillarité), Bull. Soc. franç. de dermat. et syph. **41**:884, 1934.

red blood cells and formation of pigment granules. There was almost complete dissociation of the basal layer of the epidermis.

In the discussion which followed the presentation of the patient Gougerot and Blum stated that they believed the condition to be a hemorrhagic, pigmented type of parapsoriasis accompanied by capillaritis. They cited the opinion expressed by Brocq, Blaschko and Arndt and by Juliusberg,[14] which is that a punctiform hemorrhagic reaction, especially following trauma to the lesions, is more or less characteristic of the disease. Civatte and Simon also emphasized the fact that fragility of the blood vessels may be considered a clinical sign in the plaque type of parapsoriasis. Such scant observation does not permit any conclusions to be drawn concerning the differentiation from purpuric pigmented lichenoid dermatitis. Gougerot and Blum admitted that the condition in this case very nearly fitted their conception of purpuric pigmented lichenoid dermatitis.

SUMMARY

Purpuric pigmented lichenoid dermatitis is a rather definite condition morphologically. After a review of the recorded cases and a consideration of the patients for whom we made that diagnosis, we feel that at the present time the name will serve very well to label the condition. Having seen a few cases of reaction to arsphenamine that resulted in a similar eruption and at times having seen small areas in generalized nonspecific dermatosis which resembled purpuric pigmented lichenoid dermatitis, we believe that the eruption will not prove to have a specific etiology. It seems as though it were a type of reaction due to circulating noxae. The individual lesions certainly resemble the component parts of Schamberg's disease. The fragility of the blood vessels, the red blood corpuscles in the infiltrate and the gradation of color point to an eruption dependent on an irritation which affects the blood vessels and on the changes which ensue.

Although one must look on Schamberg's disease as being confined to the lower part of the legs in nearly every case, one must keep in mind that Schamberg's first patient had the eruption also on the wrist. Differentiation of the individual lesions must be made with great care. In Schamberg's disease there are rust-colored macules of varying size, occurring definitely in or under the skin and having no papular elevations, while in purpuric pigmented lichenoid dermatitis the individual lesions are bright red pinpoint puncta or minute papules, slightly elevated and often grouped in irregularly outlined plaques. The two conditions are almost similar, but there is enough difference to justify one's according a place to this new condition.

14. Juliusberg, F.: Die Brocqsche Krankheit, in Jadassohn, J.: Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, 1928, vol. 7, p. 329.

PSORIASIS WITH BULLAE

REPORT OF A CASE

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NEW YORK

We recently observed and studied a case of psoriasis in which vesicles and bullae as well as papulosquamous lesions made up the eruption. After watching the case, it was apparent that the vesicular and bullous elements were not coincidental but actually part of the psoriatic eruption. There were no pustular lesions. The extreme rarity of the condition is, we believe, sufficient reason for reporting this case.

REPORT OF CASE

History.—G. S., a 10 year old boy born in the United States, was admitted to the dermatologic clinic of the Beth Israel Hospital in December 1933, complaining of a cutaneous eruption. The family history was essentially irrelevant. In early childhood the boy had had pertussis, chickenpox and measles.

The condition developed in August 1933 with the appearance of a circinate lesion on the anterior surface of each thigh. The mother thought the lesions were "ringworm" sores and treated them with applications of tincture of iodine. They disappeared, and the child remained free from them for one month, after which the condition recurred and appeared as a generalized eruption. He was treated in the clinic until April 4, 1934, without much success. During this period there was disappearance of some of the lesions, followed quickly by the appearance of a new crop. On April 9 the patient was admitted to the hospital for further study.

Examination and Course.—A general physical examination gave negative results. There were no apparent foci of infection. Dermatologic examination revealed a generalized eruption, most marked on the extremities. On the cheeks and chin and around the eyes there were discrete vesicular and papulovesicular lesions the size of a pinhead. One on the chin, which had been present for only four days, showed clearing in the center with a raised, red, scaling periphery. Most of the discrete lesions over the rest of the body were vesicles, bullae, papulovesicles and papules. The vesicular and bullous elements showed clearing in the center. In these central areas the skin was brownish, slightly wrinkled and in some lesions slightly scaly. The circinate lesions varied in size from that of a large pinhead to that of a 10 cent piece. On the elbows were groups of papulosquamous lesions which were typical of psoriasis. Removal of the scales

Fig. 1.—Vesicles and bullae on the palms, in addition to the scaling lesions.

Fig. 2.—The lesions on and near the elbow are typical of psoriasis.

from these lesions revealed bleeding points. On the buttocks were gyrate forms with circinate lesions of various sizes within their boundaries. The chest, abdomen and back, which had been covered by the eruption, were comparatively clear on the day of the patient's admission to the hospital. The eruption of the hands and feet had a superficial resemblance to dermatophytosis. Closer examination, however, showed that these vesicles and bullae quickly dried in the center, leaving raised circinate lesions with crusted or scaly borders. The nails were not involved. Several days after admission to the hospital papulosquamous

Fig. 3.—The various stages in the evolution of the vesicles and bullae are evident. Note the tendency to drying and scaling in the centers of these lesions. The superficial resemblance to dermatophytosis is striking.

lesions appeared on the back of the neck and extended up into the scalp. Within three weeks, with bland treatment, the eruption was practically gone.

The patient was discharged from the hospital on April 30. One week later he returned to the clinic with a mild recurrence of generalized papular and papulosquamous lesions. A bland ointment was applied, and in two weeks the eruption had again disappeared. Examination on September 25 did not reveal any evidence of a recurrence. On the forearms, buttocks and legs were light brown pigmented

areas at the sites of the old eruption. At no time during the course of the eruption was there any itching.

Laboratory Observations.—Routine examination of the urine yielded negative results, as did examinations for bromides and iodides. Two blood counts showed, respectively, the presence of 13 and 12 per cent eosinophils but were normal otherwise. Chemical analysis of the blood revealed: carbon dioxide, 1.8 per cent; dextrose, 121 mg. per hundred cubic centimeters; urea nitrogen, 14 mg.; nonprotein nitrogen, 31 mg.; creatinine, 1 mg.; cholesterol, 182 mg.; uric acid, 3.6 mg.;

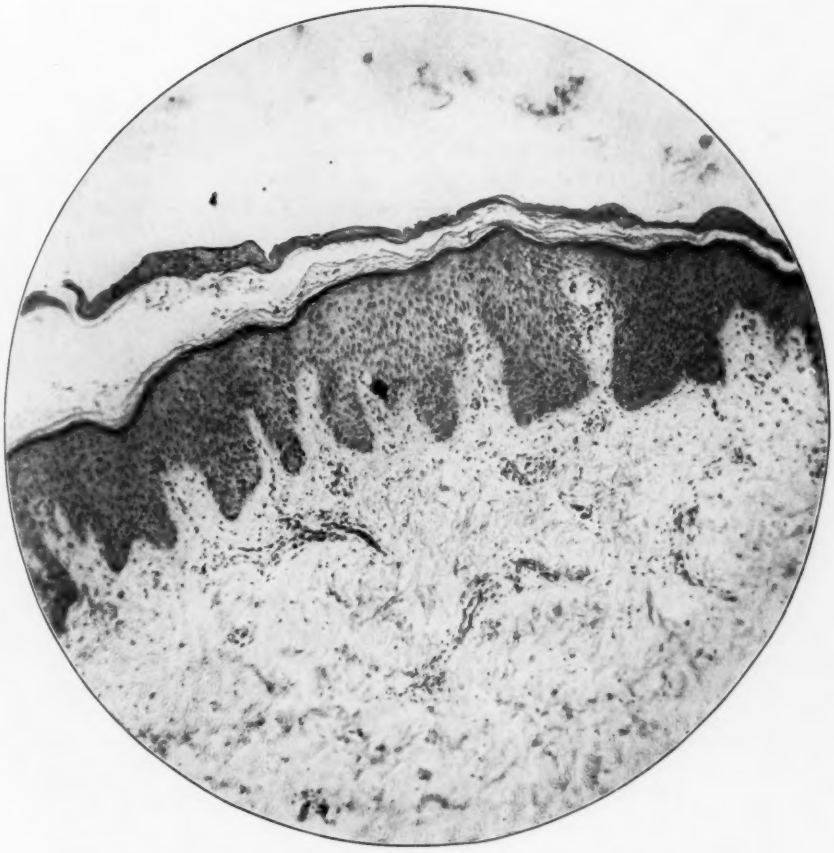

Fig. 4.—A section (low power) of a papular lesion of the buttock.

chlorides, 460 mg.; calcium, 10 mg., and phosphorus, 4 mg. The Wassermann reaction of the blood was negative. The basal metabolic rate was minus 5. Intradermal injections of trichophytin and levurine gave negative results. Serum withdrawn from the bullae and reinjected intradermally produced no reaction. Roofs of vesicles and bullae, serum from these lesions and scales were placed in Sabouraud's medium and caused no growth in any tube. A blood culture on Sabouraud's medium showed no growth. Ordinary blood cultures were negative.

Microscopic Examination.—A papular lesion of the right buttock, a dried bullous lesion of the right leg and a papulosquamous lesion of the left arm were

removed for histologic study. Many serial sections were made, and the slides were studied by Dr. David L. Satenstein. He reported the following observations:

Papular Lesions of the Buttock: The epidermis was thickened, in part owing to acanthosis and in part owing to both interstitial and parenchymatous edema. Acanthosis predominated. Some of the rete pegs were broadened, some were elongated and some were narrowed. Most of the basal cell layer was intact, and in a few zones there was some disorganization. There was little of the cellular element of the cutis present in the epidermis proper. At the edge of the section there was considerable spongiosis, with multilocular vesicles high up underneath the parakeratotic horny layer. There was some parakeratosis, part of which contained some granules which took the basic dye. The papillary bodies for the greater part were swollen, the size and shape depending on the size and shape of the rete pegs. In these papillary bodies dilated capillaries were noted, with a few cellular elements in some and considerable disorganization of the collagen in a number of them. In the subepidermal zone the collagen bundles were also somewhat disorganized. In the remaining layer of the cutis there was well developed interstitial edema. The vessels of the upper layer of the cutis were moderately dilated, the walls of the vessels being somewhat edematous. There were dilatation of the perivascular lymph spaces and somewhat sparse cellular infiltration. The infiltrating cells were predominantly of the small lymphocytic series.

The entire section represented various stages of development of a psoriatic lesion.

Dried Bullous Lesion of the Leg: The greater part of the pathologic process involved the upper layer of the cutis, the pars papillaris and the epidermis. The epidermis was irregularly thickened, the result in some measure of moderate acanthosis but mainly the result of edema. Edema was most marked in the middle and upper portion of the epidermis. In some areas the rete pegs were somewhat indicated but were not pronounced. The basal portion of the epidermis was to a great extent intact and unaffected. In some places there were some moderate interstitial edema, some spongiosis (not marked) and large unilocular cavities of various sizes. The majority of the cavities were practically subcorneal and extended into the midportion of the epidermis. The floor of the largest cavity was fairly sharply encircled by compressed prickle cells, and in some of the smaller ones the floor was encircled by loosely arranged prickle cells. The contents of the cavities consisted of a few small deeply stained cells and some finely granular fibrin. The roofs of the cavities were formed by the horny layer. The granular layer extending across the greater part of the section was indicated by a single layer of cells. In a few spots there were two or three rows of cells. In one portion toward the middle of the section there was some parakeratosis, underneath which there was no granular layer.

The horny layer at the outer parts of the section was slightly laminated and in close apposition to the surface epidermis. In the central portion the horny layer was somewhat raised, appearing somewhat irregular, and there was an irregularly shaped cavity between the horny layer and the underlying epidermis. Part of the cavity was empty, and the other part contained some loosely arranged horny cells and granular fibrin. Over the central portion of the cavity, the horny cell layer was somewhat separated and parakeratotic and contained some homogeneous fluid.

In the upper layer of the cutis there was well developed interstitial edema resulting in a dissociation of the collagen fibers with some granular breaking down of some of these fibers. The blood vessels were moderately dilated, and there was a somewhat sparse infiltration of small cells, partly perivascular and partly diffuse.

The entire histologic evidence suggested a process which had been present for some time associated with a sudden outpouring of fluid resulting in the formation of superficial vesicles and the lifting up of the horny layer.

The picture was not that which one ordinarily sees in cases of chronic eczema. Parts of the picture were similar to the descriptions of cases recently recorded under the name of vesicular or pustular psoriasis. In this instance there were no polymorphonuclear leukocytes in the cavities.

Papulosquamous Lesion of the Arm: At one edge of the section there was considerable irregular acanthosis, the remaining epidermis being fairly normal. At this edge there was some irregular distribution of the granular layer, which in some places was somewhat increased and in others absent. Overlying this portion was a horny layer which was partly edematous and partly parakeratotic. There was no formation of vesicles and very little edema. In occasional zones there was moderate interstitial edema of the lower portion of the epidermis. In the upper layer of the cutis there was some interstitial edema causing a dissociation of the fibers. There was also some interstitial edema of the deeper layer of the cutis. The papillary capillaries and the vessels of the upper layer of the cutis were dilated. About the perivascular lymphatic spaces there was some lymphocytic infiltration.

From the diagnostic point of view it would be rather difficult to fit this lesion in with a classic picture of psoriasis, and yet the picture was not that of a simple dermatitis. The edema of the papillary bodies, the dilatation of the papillary vessels, the irregular arrangement of the granular layer and the presence of parakeratosis might well fit in with a picture of retrogressing psoriasis, though a positive diagnosis could not be established.

Summary.—The papular lesion of the buttock could have been readily labeled psoriasis. The section of the dried bullous lesion might well have been part of a retrogressing lesion in which there was a somewhat sudden outpouring of fluid resulting in edema, with the development of epidermal and subcorneal vesicles. The papulosquamous lesion of the arm suggested psoriasis but could not be absolutely diagnosed.

COMMENT

From the older, orthodox point of view, psoriasis is essentially a papulosquamous disease. In fact, Stelwagon [1] stated in 1916 that "psoriasis is always a dry, scaly-papular eruption—oozing or liquid exudation never occurs, and such other lesions as vesicles, pustules, etc., are never observed." Since then, of course, a much broader conception of psoriasis has been generally accepted by most dermatologists.

When this case first came to our attention, the circinate scaling lesions and the subsequent appearance of papular and vesicular lesions caused us to make a tentative diagnosis of dermatophytosis with dermatophytids. When, in addition, a fungus was found microscopically in the scales from one of the lesions, this diagnosis seemed tenable. However, the negative reaction to trichophytin and the numerous subsequent negative

1. Stelwagon, H. W.: Treatise on Diseases of the Skin for the Use of Advanced Students and Practitioners, ed. 8, Philadelphia, W. B. Saunders Company, 1916.

results of microscopic examinations and cultures forced us to abandon this diagnosis. We now doubt the accuracy of the original finding of mycelia.

On further observation we noted that the papular portion of the eruption, especially that part covering the elbows, was becoming more definitely characteristic of psoriasis. On the face, neck and buttocks the gyrate and circinate papulosquamous forms gave the distinct impression of microcircinate psoriasis (Jadassohn [2]).

The histologic report by Dr. Satenstein was not inconsistent with the diagnosis of psoriasis.

In this connection it is pertinent to quote Highman,[3] who stated that "in inflammations of the skin we rarely find either a purely desquamating or a purely vesicular lesion. The two are invariably combined, the one dominating in what we are disposed to call scaling dermatoses and the other in vesicular dermatoses. In frankly vesicular dermatitis there is always a great element of scaling, and in the other type we can demonstrate vesiculation under the microscope." It is logical, therefore, that when an intensification and accentuation of the usual histologic picture occur the clinical features of psoriasis must correspondingly change.

Haslund [4] emphasized the fact that the outpouring of serous exudate may be of sufficient force to separate some of the rete cells, compressing them and thus forming enlarged intercellular spaces. He found that this intensification of the serous exudation was almost always associated with marked outpouring of polymorphonuclear cells, which filled the resultant spaces. In our case this cellular outpouring was absent. Haslund further believed that the serous and cellular exudate may be so marked that the psoriatic papule is covered with material that partakes more of the nature of a crust than of a scale.

The practical enlargement of this concept accounts for the acceptance of pustular psoriasis as a variant of psoriasis vulgaris. Ebert [5] gave an adequate résumé of the literature pertaining to pustular psoriasis, and for our purposes it is not necessary to review the cases of von Zumbusch,[6] Schaefer,[7] Barber [8] and others. Suffice it to say that when the microscopic Munro-Sabouraud abscesses become sufficiently enlarged, one finds a clinical case of pustular psoriasis similar to those of the aforementioned authors.

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2. Jadassohn, J.: Zentralbl. f. Haut- u. Geschlechtskr. **11**:282, 1924.
3. Highman, W. J., in discussion on Ebert.[5]
4. Haslund, P.: Arch. f. Dermat. u. Syph. **114**:427, 1912.
5. Ebert, M. H.: A Psoriasiform Eruption with Pustular Exacerbations, Arch. Dermat. & Syph. **27**:933 (June) 1933.
6. von Zumbusch, L.: Arch. f. Dermat. u. Syph. **99**:335, 1910.
7. Schaefer, R.: Dermat. Ztschr. **33**:49, 1921.
8. Barber, H. W.: Brit. J. Dermat. **42**:500, 1930.

A case of bullous psoriasis was reported by Kissmeyer [9] in which there was evidently a further intensification of the mechanism operating in the reported cases of psoriasis pustulosa. Leukocytes were present in the bullae, but they were absent in our case.

Rosen reported a case in which a woman aged 39 suffered from a recurring eruption made up of vesicular lesions with a tendency to the formation of a crust, lichenified plaques and a single scaly patch. He believed the condition to be psoriasis, "because of the erythematous and firm character of the involved area, the micaceous scaling and the occasional deep-seated papulo-vesicles which rupture and are covered with a crust. Further, the persistence of the lesions, the resistance to all forms of therapy and the presence of clinically characteristic psoriatic lesions. . . ."

From a clinical standpoint the papulosquamous lesions of the elbows and buttocks were typically those of psoriasis. The histologic picture of the lesion of the buttock fits in readily with that of psoriasis. The question then develops as to the interpretation of the vesicular and bullous lesions. It was evident from our observation of the case that we were dealing with one cutaneous disease. When the eruption cleared up both the papular and the bullous elements disappeared at the same time and responded to the same treatment. The evolution of the bullae into circinate lesions with infiltrated and crusted borders is different from the course of the bullae seen in toxic erythema. Circinate and crusted lesions are not uncommon in psoriasis, and such lesions occurring together with typical psoriatic manifestations make it logical to consider the whole picture that of psoriasis with bullae. The histologic picture of one of the bullous lesions, as described by Dr. Satenstein, is not inconsistent, with the exception of the absence of leukocytes from the cavities, with the histologic picture described in many reported cases of pustular psoriasis. It might be pointed out also that, as in pustular psoriasis, all the cultures from the various lesions in our case were sterile.

SUMMARY

A case of psoriasis with bullae is reported.

All the laboratory examinations gave negative results.

The resemblance of this condition to pustular psoriasis is emphasized.

Histologic examinations suggested a diagnosis of psoriasis.

It is not unreasonable to classify the condition in this case as another variant of psoriasis.

9. Kissmeyer: Dermat. Ztschr. **24**:397, 1917.

LIP-STICK DERMATITIS

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PITTSBURGH

The paucity of literature on dermatitis due to lip-stick does not indicate that the condition is rare, for the rôle that cosmetics generally play in the development of dermatitis is difficult to evaluate. As a routine I have questioned women in regard to irritation about the lips and have been surprised at the number who had noted irritation from certain brands of lip-stick which had disappeared after the substitution of another brand. It is in the exceptional case that the dermatologist is consulted.

Dermatitis of the lips (cheilitis) produced by lip-stick has been mentioned by Lain,[1] Miller and Taussig,[2] Sutton,[3] Ormsby [4] and others. The specific factor in its production has not been definitely recognized, as the dye, the perfume and the various bases have been suspected.

It is difficult to predict when a substance in constant use may act as an irritant. Sulzberger and Wise [5] have shown that in cases of contact dermatitis due to butesin picrate there is a period of incubation of from twelve days to several years, which may be compared to the interval occurring in serum sickness. Persons (exclusive of atopic or hypersensitive patients) vary in their response to a dermal irritant, and the fact that a substance is commonly and frequently used does not exclude it from suspicion as an irritant. Gradual sensitization takes place, and the time required is directly proportional to the concentration and frequency of the use of the offending agent (period of latency or incubation). The substances that may act as an irritant are many.[6]

Bloch [7] recognized a "silent" form of sensitization; i. e., a person can be sensitized to a substance without showing appreciable clinical manifestations at any time, a gradual desensitization occurring until exhaustion develops at the site.

From the Pittsburgh Skin and Cancer Foundation.

1. Lain, E. S.: Cosmetic Eruptions, South. M. J. **25**:718 (July) 1932.

2. Miller, J. H., and Taussig, L. R.: Lip Stick Dermatitis Due to Carthamine and Eosin, J. A. M. A. **84**:1999 (June 27) 1925.

3. Sutton, Richard L.: Diseases of the Skin, St. Louis, C. V. Mosby Company, 1934.

4. Ormsby, Oliver S.: Diseases of the Skin, Philadelphia, Lea & Febiger, 1934.

5. Sulzberger, Marion B., and Wise, F.: Drug Eruptions: II. Dermatitis Eczematosa Due to Drugs, Arch. Dermat. & Syph. **28**:461 (Oct.) 1933.

6. Weber, Leonard F.: A List of Cutaneous Irritants, Arch. Dermat. & Syph. **21**:761 (May) 1930.

7. Bloch, Bruno, quoted by Beerman.[11]

The underlying factor in cosmetic dermatitis may be either idiosyncratic or the result of direct chemical irritation or both. Sensitivity to drugs may develop in any one; all that is required, for the most part, is continued use of a substance for a long time so that the cumulative irritation may become of sufficient strength to cause the skin to rebel (saturation dose).

In contact dermatitis localized sensitization must occur before a reaction will be elicited (sensitizing exposure).[8] A chemical interaction may often be produced by the various substances placed on the skin.

Simon and Rackemann[9] aptly raised the question whether substances act directly or whether they create or excite production in the skin of a common substance (present in all the dermatitdes), which in turn produces the dermatitis. The reaction in contact dermatitis is not specific, and it is nontoxic. Multiple sensitivity may occur. Local antibodies occur as demonstrated by the Urbach-Königston, the Peruts or the Lehner-Rajk method for passive transfer of fluid from a blister. Systemic antibodies do not occur in contact dermatitis, as the Prausnitz-Küstner reaction is negative.

REPORT OF A CASE

Mrs. L. C., aged 36, who presented herself in February 1934, had an itchy dermatitis about the lips of eight months' duration. Surrounding the vermilion borders of the lips the skin showed subacute and scaly dermatitis, which was definitely demarcated. Various salves and lotions had been applied for relief, but these procedures had apparently aggravated rather than alleviated the condition.

The history suggested that the lip-stick might be at fault. She carried two shades of lip-stick in separate containers, supposedly of different brands. Both forearms were cleansed, and the lip-stick was rubbed into the skin. This was covered with waxed paper; an occlusive dressing was applied, and the reaction was observed in twenty-four hours. Marked dermatitis with vesiculation was present on both sites to which the lip-sticks had been applied.

As the lip-sticks were in separate containers and were thought to be of different brands, both brands were placed under suspicion. Later, however, it was found that the lip-sticks were of the same brand but of different shades. In order to eliminate any possible error new lip-sticks were purchased of the two brands in question, and the patch tests were reapplied. The result was positive for only the one brand of lip-stick that the patient had been carrying.

The dermatitis of the lips cleared in ten days after the discontinuance of the use of the lip-stick and the application of a soothing cream. Later, when the lip-stick was again applied there was a marked recurrence of the dermatitis within forty-eight hours. Various brands of lip-stick were then applied to the arm as patch tests. A positive response was obtained to only one other lip-stick. Patch tests were made on forty-two other women, with a negative response in all.

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8. Jadassohn, J., quoted by Keston, Beatrice, and Laszlo, Elizabeth: Dermatitis Due to Sensitization to Contact Substances: Dermatitis Venenata, Occupational Dermatitis, Arch. Dermat. & Syph. **23**:221 (Feb.) 1931.

9. Simon, Frank A., and Rackemann, Francis M.: The Development of Hypersensitiveness in Man Following Intradermal Injection of Antigen, J. Allergy **5**:439 (July) 1934.

MANUFACTURE OF A LIP-STICK [10]

The following waxes, fatty alcohols and fatty acids are commonly employed in various proportions by the manufacturers of lip-stick: paraffin, yellow wax, carnauba, spermaceti, oil of theobroma, stearic acid, cetyl alcohol, tri-ethanolamine stearate and glyceryl mono-stearate. The lubricants include petrolatum, hydrogenated cottonseed oil and benzoinated lard. The emollient agents include hydrous wool fat and its absorption bases, castor oil and oil of theobroma, which is also a lubricant. The castor oil, in addition to being an excellent lubricant and emollient, acts as a solvent. A di-brom or tetra-brom derivative of fluorescein is used to set the color and make it permanent.

The dyes used in the manufacture of lip-stick are of vegetable and aniline origin. Some aniline dyes used include eosin, rhodamine B, erythrosin and geranium red. Those of vegetable origin are burnt sienna, carthamus (safflower), carmine (cochineal) cudbear, fuchsin and phloxin.

Fig. 1.—Dermatitis of the vermilion border and adjacent border of the lips due to a form of lip-stick.

The following basic formula is used in the manufacture of lip-stick:

	Percentage
White wax	30.0
Hydrogenated cottonseed oil	8.0
Oil of theobroma	7.0
Castor oil (tasteless)	6.0
Absorption base of hydrous wool fat	20.0
White petrolatum (short fiber type)	15.0
Perfume	0.9
Preservative	0.1
Di-brom or tetra-brom derivative of fluorescein	3.0
Coloring matter	10.0

10. Lipstick Manufacture, Drug & Cosmet. Indust. **35**:251 (Sept.) 1934.

About 1 per cent of the preparation consists of the perfume component, and 10 per cent, of the coloring matter.

As a substitute for the dyes either the di-brom or the tetra-brom derivative of fluorescin is used to give a permanent color. This is soluble only in castor oil. If there is an excess of either of these substances it is believed that either the di-bromoricinoleate which is formed or the di-bromfluorescein remaining causes the irritation to the skin.

Because the dye contained in the patient's lip-stick was suspected, tests of solutions of the following aniline dyes were made both on the patient and on forty-eight persons used as controls, with negative results in all cases:

1. Scarlet—oil-soluble
2. Malachite green—water-soluble
3. Green—oil-soluble.
4. Indigo carmine—water-soluble and alcohol-soluble
5. Red—oil-soluble
6. Methyl violet—water-soluble and alcohol-soluble

I then made patch tests of the following substances supplied by the manufacturer, which represent the various stages in the manufacture of the lip-stick which the patient was using:

1. Lip-stick base (a mixture of fats and waxes)
2. Lip-stick base and the perfume in the lip-stick
3. Lip-stick base and the insoluble part of the coloring matter (lakes); no perfume
4. Lip-stick base and the soluble coloring matter, but no perfume
5. Finished lip-stick (rose-coral shade) but no perfume
6. Finished lip-stick (rose-coral shade) with a different perfume than that contained in 2

The patient responded only to the lip-stick base and perfume, the reaction consisting in a vesicular and erythematous patch which persisted as dermatitis and disappeared in two weeks.

This reaction incriminated the perfume in the lip-stick. I then applied as patch tests the following components of the perfume, which are some of the synthetic substances blended with the basic oils of the perfume:

1. Iris concrete
2. Alpha ionone
3. Methyl ionone
4. Rose Bulgarian
5. Methyl heptine carbonate
6. Violet flowers, synthetic

The patient showed a marked reaction to the methyl heptin carbonate, manifested as dermatitis with dermonecrosis.

As controls thirty-eight women who used lip-stick were tested with these ingredients of the perfume, and 50 per cent responded to the irritation of the methyl heptin carbonate. Ten men were also tested, and four showed irritation from the same ingredient.

The following animal substances that are blended with the synthetic and the absolute components of perfume were used in patch tests on thirty-eight women and fourteen men:

1. Ambergris
2. Civet
3. Castor
4. Musk

A mild erythematous response was obtained to castor and to musk in two persons, but the reaction of the patient was negative.

Patch tests with castor oil and ricinoleic acid were performed on eight women besides the patient and produced negative reactions in every case.

The Prausnitz-Küstner test for passive transfer was attempted on five persons, and the reaction was negative in all instances.

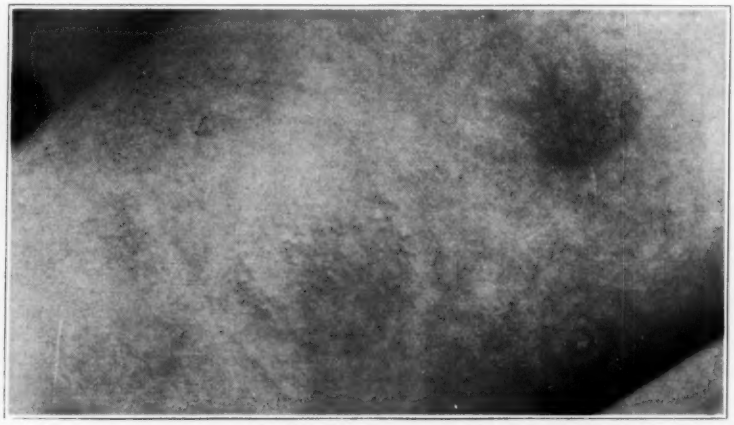

Fig. 2.—Erythematous and vesicular types of eruption in patch tests with the same lip-stick producing the dermatitis shown in figure 1.

MANUFACTURE OF PERFUMES [11]

This industry has assumed great momentum, owing to the advances made in chemistry and the simplification of the processes used in the manufacture of perfumes. The earliest people to develop skill in the manufacture of perfumes were the Arabs in the Middle Ages. The United States imports practically all its perfumes from France and Italy, which at present are the leaders in this industry. Perfumes are of complex composition. Prior to the development of the manufacture of perfumes as an industry, the animal perfumes, balsams and natural perfumes were utilized. The animal perfumes, which are costly, were developed from ambergris, civet, castor and musk. The balsams, gums

11. (*a*) Poucher, W. A.: Perfume and Cosmetic with Especial Reference to Synthetics, New York, D. Van Nostrand Company, 1923. (*b*) Parry, Ernst J.: Parry's Cyclopedia of Perfumery, Philadelphia, P. Blakiston's Son & Co., 1925.

and oleoresins contain a small amount of highly odorous essential oils and are used in perfumes because they delay evaporation and in addition have a soft, tenacious odor.

The aroma of a natural perfume is contained in the essential oil, which exists in a free state or as a glucoside bound up in the chlorophyl. This aroma or scent has been duplicated by the recognition and development of esters, ketones and aldehydes from synthetic sources. The secret of any perfume lies in the careful blending of the synthetic perfumes with the natural oil or "absolute" of the plant. The theory of specific esters is supported by most perfumers. The predominating ester may be calculated and determined for each aroma. The genuineness of a perfume is at times difficult to determine, except by experienced perfumers.

Three methods are used for "winning" the oil from the plant, namely, distillation, expression and extraction. The utilization of the method of choice depends on the part of the flower in which the oil exists and on the preservation, not the modification, of its aroma.

Distillation is the process used for vegetable organisms, excepting most fruits and some flowers. Expression by a cold process is used to obtain the essential oil from the peels of bergamot, lemon, lime, orange, etc. Extraction is used in the more delicate processes and avoids the destruction of the oil which occurs with the other methods. "Absolutes" are the most highly concentrated of the floral forms and are pure nonalcoholic vegetable products free from the addition of synthetic substances and coloring matter.

Fixation is one of the most important stages in the manufacture of perfumes. This art depends on the careful selection of substances which when blended with the more volatile constituents of the perfume will prevent their evaporation and at the same time retain the predominating note of their fragrance. Only through experience are perfumers able to choose the fixatives that will give complete harmony of the various constituents employed. For example, the building up of a perfume may be as follows:

1. An animal perfume, such as musk, civet, ambergris or castor, is added to the synthetic portion to impart "warmth and life" and to improve the aroma by softening the harshness caused by the synthetic component.

2. The addition of a small quantity of a substance, such as verbena, bergamot or *bois de rose*, produces a sweet and pleasant fragrance.

3. A suitable quantity is added of the natural absolute, which has the fresh and glowing characteristics of the predominating flowery note.

Many of the fixatives, if those derived from animal sources are considered, have a disagreeable odor, but when employed in dilutions they acquire a pleasant fragrance.

Hundreds of synthetic substances have been developed the aroma of which simulates that of the natural perfumes. These are mostly the

esters, ketones and aldehydes of the coal tar products. The ionones, methyl heptin carbonate and the alcohols are the most important. Ambergris is the most important animal substance used.

The finished perfume is a solution of the artificial flower oil in about 80 per cent alcohol to which some of the natural oil is added. The secret of any perfume lies in its lasting odor (provided by the animal fixatives, which in addition give it warmth), the slowness of evaporation (which the oleoresins and balsams provide) and the lack of staining properties (dependent on the type of alcohols used and on filtration).

Ambergris is a pathologic secretion of the sperm whale, which is found floating on the sea, on the sands or in the dead whale. It is used in the form of an infusion in 90 per cent alcohol, usually in a strength of about 5 per cent. It has very high power as a fixative.

The alcohols are of the monohydric or primary type, but other alcohols are included in many of the essential oils. The alcohols used by the perfumer must be absolutely free from odor and secondary constituents. The perfumer uses the lowest strength compatible with efficiency in his products, and he tests the alcohol for impurities and for its strength in the finished products.

Methyl heptine carbonate is the parent substance of a new and important series of artificial perfumes. The preparation is painstaking and requires the most delicate management and technic. The initial material in its preparation is ricinoleic acid. This is heated under pressure and gives off an aldehyde containing seven atoms of carbon. The distillate is then chlorinated by means of phosphoruspenta-chloride. The resulting di-chloride saponified with potassium hydroxide gives heptine. If this substance is allowed to react with sodium hydroxide and then with chlor carbonic methyl ester, methyl heptine carbonate will be formed.[11b] The following reactions are involved in the process:

A. (Castor oil) $C_{18}H_{34}O_3 \rightarrow C_{10}H_{19}CO_2H$ (a by-product)
(Ricinoleic acid) (Undecylenic acid)

↓

B. $CH_3\ (CH_2)_5\ COH\ PCl_5$
Heptanal

↓

C. $CH_3\ (CH_2)_5\ CHCl_2$
Di-chlorheptane

↓

D. $CH_3\ (CH_2)_4\ C:\ CH$
Heptine

↓

E. $CH_3\ (CH_2)_4\ C:\ C\ Na$
Heptine sodium

↓

F. $CH_3\ (CH_2)_4\ C:\ C\ CO_2\ CH_3$
Methyl heptine carbonate

Methyl heptine carbonate is a colorless, mobile liquid, boiling at 109 C. under a pressure of 20 mm. It has a specific gravity of 0.9524. When pure it has a strong, sharp, penetrating and disagreeable odor. When diluted it has the fragrance of fresh violets. With the ionines it replaces the violet extracts.

COMMENT

The specific etiologic factor in lip-stick dermatitis may be difficult to determine, owing to the complexity of the ingredients that constitute the formula; but there are other factors that may be conducive to its development, such as an inheritable personal factor (idiosyncrasy), trauma of the skin with bacterial contamination, diet, food, saliva and previous irritation of the susceptible site.

Beerman [12] has shown that in dermatitis due to hatbands there is an interplay of multiple etiologic factors, namely, the manufacture of the leather of the hatband, the dyestuffs and, in addition, local and focal fungous infection.

The problem confronting one was which of the ingredients of the lip-stick acted as the irritant. Perfumes per se, except as noted in cases of berlock dermatitis, have not been regarded as dermal irritants. In the use of the various perfumes with ultraviolet irradiation to produce pigmentation in cases of vitiligo, I have found more irritation due to Shalimar than to other perfumes.

Most reports [13] of cases of perfume dermatitis deal with the peculiar pigmentation of the skin as a result of the action of natural sunlight on perfume (berlock dermatitis). Attempts to reproduce this pigmentation with the use of artificial ultraviolet radiation have not had universal success. Oil of bergamot (synthetic or natural), sunlight, sweat and alcohol, alone or in combination, have been incriminated as factors in the resulting dermatitis, with or without the pigmentation.

Goodman's [14] experiments showed that the pigmentation due to sunlight is much darker and more lasting than that following exposure to the quartz mercury vapor arc lamp. He stated that a factor in the

12. Beerman, H.: Leather Dermatitis, Arch. Dermat. & Syph. **29**:671 (May) 1934.

13. (*a*) Goodman, Herman: Perfume Dermatitis: Case Report with a Review of the Literature and Bibliography, Brit. J. Dermat. **63**:177 (Jan.) 1931. (*b*) Gross, Paul, and Robinson, L. B.: Unusual Dermatitis and Pigmentation Following Use of Perfume, Arch. Dermat. & Syph. **21**:637 (April) 1930. (*c*) Downing, J. G.: Pigmentation from Perfume; "Berlock" Dermatitis, New England J. Med. **207**:660 (Oct. 13) 1932.

14. Goodman, Herman: Perfume Dermatitis: Case Report with Review of Literature and Bibliography, Am. J. Phys. Therapy **9**:16 (April) 1932; footnote 13*a*.

production of the dermatitis may be a difference between the synthetic and the natural oil of bergamot, which is contained in eau de cologne.

Gross and Robinson [13b] expressed the belief that hypersensitivity or idiosyncrasy and the frequency of application and exposure to the sun, rather than actinic irradiation, are the underlying factors in the production of berlock dermatitis.

The question of whether a dye can act as a dermal irritant is pertinent. In cases of shoe-dye dermatitis [15] the solvent for the dye rather than the dye is at fault. White [16] expressed the belief that the farther the process of the dye-making is from the completion of its finished product the less likely the dye is to act as an irritant. He stated that the solvent rather than the dye is the irritant. Cummer [17] was not certain that in a case of toilet-seat dermatitis it was the solvent rather than the dye which produced the irritation. Miller and Taussig [2] reported a case of cheilitis due to lip rouge which contained carmine (an aniline dye) in alcoholic solution. Whether they actually found this dye present or assumed it to be is not stated. Carleton,[18] on the other hand, stated that lip-stick dermatitis is rare and that it is produced by the aniline dye. It is a recognized fact that some aniline dyes (scarlet red) [16] will produce irritation, erosion and sometimes systemic effects when applied to the skin locally for a long time. No doubt, the strength of the dye should be much greater than that used in the lip-stick.

I have been informed by the manufacturer of the lip-stick that the dye used in their lip-sticks is of vegetable origin and that synthetic dyes are rarely used.

CONCLUSION

Dermatitis of the lips produced by lip-stick is not uncommon.

Perfume was found to be the irritant in a case of lip-stick dermatitis, and methyl heptine carbonate, a product of castor oil, was found to be the specific factor.

An account is given of the processes in the manufacture of lip-stick and perfume.

5050 Jenkins Building.

15. Harry, R. E.: Report of Cases of Poisoning Due to Shoe Dye, Nebraska M. J. **19**:455 (Dec.) 1934.

16. White, R. P.: The Dermatergoses or Occupational Affections of the Skin, New York, Paul B. Hoeber, Inc., 1929.

17. Cummer, Clyde L.: "Toilet-Seat Dermatitis" Produced by a Red Stain: Possibility of a Sudan Stain as Causative Factor, Arch. Dermat. & Syph. **27**:976 (June) 1933.

18. Carleton, Alice: Use and Dangers of Cosmetics, Brit. M. J. **1**:999 (June 10) 1933.

REPRODUCTION OF PATHOLOGIC SPECIMENS IN DERMATOLOGIC PRACTICE BY MAKING WAX MOULAGES

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Many agents are used to reproduce pathologic changes in living tissue, such as schematic drawings in black and white, photographs, cuts, colored plates and motion pictures. Needless to say, the most realistic means of demonstrating these changes would be to excise a lesion and study it grossly in situ. However, this method is unsatisfactory because the pathologic details which characterize the growth of the lesion soon disappear when it is removed from its host. Even the most carefully preserved pathologic specimens lose their definition and color, as well as their consistency and size, shortly after being immersed in preservatives.

The art of making wax moulages has been practiced in one form or another for many years, especially in Europe. This procedure portrays exactly the true pathologic changes because it affords an exact reproduction, in detail, of the lesion standing out in bold relief. With the help of the artist the lesion can be duplicated to the minutest detail as it retrogresses from the normal, taking on malignant characteristics, such as chronic inflammation, sharply defined or irregular borders and signs of cystic degeneration and ulceration.

Douglas,[1] medical illustrator in the Montreal General Hospital, has done some beautiful work in this field under the direction of Dr. L. J. Rhea and has written extensively on the subject. Douglas applied the process, originated by Wallis,[2] which has been used so skilfully at the Army Medical Museum of Washington. At the Century of Progress Exposition, which was held in Chicago recently, there were wonderful moulages in the medical exhibit, many of which were produced in the department of cancer of the Michael Reese Hospital, Chicago, showing the lesions before and after treatment with roentgen radiation, radium and electrosurgery. The artists carefully and painstakingly portrayed the cancerous growth in all its stages of pathologic degeneration—the slough, the swelling, the edema and the red blood from atypical sinuses.

The making of moulages is of aid to the dermatologist because lesions of the skin are of such consistency that they respond to this method

1. Douglas, Hortense P. A.: J. Tech. Methods **12**:52, 1929.
2. Wallis, J. Frank: The Moulage as a Record Employed at the Army Medical Museum, J. A. M. A. **73**:1499 (Nov. 15) 1919.

easily, in contrast to intra-abdominal lesions, which are more difficult to reproduce because of the softnesss of the structures. The surgeon must fix the soft growths in formaldehyde before a negative impression is made; thus he destroys the finer characteristics.

The greatest obstacle to making a perfect impression is the undercutting, especially in soft tissues. In fact, correct filling of the undercut areas is so important a factor in producing a perfect impression that certain companies have made a plaster which is elastic and which will give, contract and expand. Thus a negative can be produced which will be an exact reproduction of the original lesion with the undercut areas intact. The material for the negative is called negocoll.[3] As prepared by Poller,[4] it possesses the following characteristics: 1. It can be used repeatedly, as many as three hundred times. 2. It is easy, quick and clean to handle. 3. It is elastic and permits casting of the undercuts in one piece. 4. Valuable specimens are not endangered by its use. 5. It does not stick to hair. 6. It is nonirritating to the normal skin and is aseptic. 7. It can be applied to the subject sitting, standing or reclining. 8. It produces the finest details of pores, fissures and folds.

METHOD

The lesions should be selected carefully; those with undermined, ulcerated or rolled borders are especially desirable. The lesions should be washed thoroughly with a saline solution to remove all débris and rinsed in a weak solution of sodium hydroxide. The tissue is then dried with gauze and covered with liquid petrolatum, which prevents the undercut edges and hair from sticking to the plaster. Negocoll or plaster of paris is then applied in a semisolid condition, without omitting to fill the undercut areas. Before the negocoll or the plaster is quite dry, it should be removed in toto if possible; this can be easily done with negocoll, but if the plaster negative breaks, it may be removed in pieces and reconstructed later. The most critical patient will not object to this procedure if one explains the reason for it. When making a negative cast of a face, however, one should place soft rubber tubing in the mouth to allow breathing and lubricated cotton in the nostrils and in the ears. If the cast is removed before the plaster is quite dry, the undercutting will be reproduced more beautifully.

After the negative reproduction is made, the positive is produced by filling the negative impression with a liquid wax. Devices for dental casting are used as pedestals on which to mount specimens; they have a removable false bottom, and the sides are painted with oil before the plaster is poured in. The wax is prepared in a double boiler in a water bath. The negative is removed and the reproduction of the lesion comes out intact in bold bas-relief, provided the negative has first been well lubricated.

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3. Negocoll may be obtained from the Kern Co., New York. It is rather expensive.

4. Poller, A.: Das Pollersche Uerfahren zum Abformen, Berlin, Urban & Schwarzenberg, 1931.

Gross,[5] of Western Reserve University, Cleveland, while in the laboratory of the Charity Hospital worked out a variation of this technic. He followed the routine indicated by Poller,[4] with variations. Gross, however, described a new type of negative mass which is inexpensive and easly prepared. The formula is as follows:

Material	Parts by Weight
Agar	100
Oil soap	100
Magnesium sulphate	40
Absorbent cellulose wadding [6]	800
Water	700–800

Dr. Samuel Iglauer of Cincinnati has used Poller's technic with great success. He has done some beautiful work with the German method.

A good formula for the wax used in the positive mold is as follows:

White beeswax	2	pounds (907.2 Gm.)
Paraffin	1½	pounds (880.4 Gm.)
Talcum powder	1	pound (453.6 Gm.)
Prepared cornstarch	1	pound (453.6 Gm.)
Yellow beeswax	2	ounces (56.7 Gm.)

When possible the color of the tissue proper should be dropped into the liquid wax compound. A small amount of the wax should be tinted to determine the exact color wanted before tinting the whole batch.

A wax moulage is of great aid to the student of dermatology, and by means of a moulage the dermatologist in practice may keep a permanent record of a case—a replica of the lesion exact as to size, shape, configuration and color.

SUMMARY OF TECHNIC OF MAKING WAX MOULAGES

Preparation of the Negative.—Lubricate all parts to be molded with liquid petrolatum (heavy) to prevent sticking.

Apply the negative composition to the lesion liberally. Allow to set sufficiently so that it may be removed in toto. If it cannot be removed completely, owing to much undercutting, remove it in segments and later join the sections together.

Preparation of the Positive.—Paint liquid wax on the plaster negative (which has been lubricated with liquid petrolatum), especially filling all

5. Gross, Paul: A New Negative Mass for Making Accurate Plastic Reproductions, Arch. Path. **16**:869 (Dec.) 1933.

6. The cellulose wadding from so-called sanitary napkins or pads was used.

undercut areas by brushing the wax carefully into the negative. After the mold or negative is filled completely with the wax, allow it to cool sufficiently so that the negative can be removed without destroying the definition of the undercut surfaces.

Mounting of the Moulage.—After the moulage has been made, mount it on a pedestal. I use an aluminum mold with a removable bottom and top. Make the base of the plaster of paris. While the mounting is still soft, apply the moulage of the lesion.

Painting of the Specimen.—With oil paints of good quality reproduce exactly the colors found on the lesion. Allow the paint to dry for twelve hours and then apply a coat of clear shellac to preserve the colors.

The color used are white, sienna, vermilion, black, blue and yellow, or suitable mixtures of these.

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INJURIOUS EFFECTS OF SODIUM CHLORIDE AND THEIR PREVENTION

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The discovery that the manifold intolerance reaction of an organism results from sensitization and depends on a specific reaction signifies an important advance in the field of medical science. In modern research in the field of allergy not only has the dependence of the allergic reaction on the antigen-antibody reaction been shown but it has been produced experimentally in animals and transmitted passively in human beings, achieving specific desensitization.

Precisely because of the far-reaching importance of allergy, the fact may easily be overlooked that not every intolerance reaction of an organism is based on a specific antigen-antibody reaction. This statement is illustrated in the case of the intolerance reaction which results from quantitative overdosage of stimuli and which yields the same clinical picture as the reaction based on specific sensitization. Thus, for example, all human beings will react with intolerance to abnormally large doses of arsphenamine, while only a small group of patients with special causative mechanisms will react to a therapeutic dose of arsphenamine. The individual disposition which this type of reaction demands may signify one of two things: Either commonplace stimuli (that is, stimuli which are tolerated in themselves) are transformed into abnormally strong or toxic stimuli through intermittent allergic reactive processes, or an endogenously conditioned polyvalent hypersensitivity exists toward numerous commonplace stimuli (thermal, mechanical, chemical, etc.).

Among the factors which influence the increased sensitivity of the skin, a very important one is mineral economy, as shown by the results of our experiments reported in this paper. We proceeded from the observation that a modification of the mineral economy, for instance by means of a salt-free diet or medication with calcium, will materially improve or cure numerous dermatoses.

In order to determine whether withdrawal of sodium chloride from the diet is actually a material factor in pathologic cutaneous reactions,

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we first carried out what in a sense represents a countertest. Our experimental procedure for testing the injurious effects of sodium chloride was as follows:

Seventy-two patients, of whom eighteen had urticaria, twenty chronic eczema, twelve acute eczema, sixteen neurodermatitis and six dyshidrotic eczema, were put on a salt-free diet for three days and then the system was flooded with 20 Gm. of sodium chloride daily in four doses of 5 Gm. each. In order to exclude suggestive influences as far as possible, the sodium chloride was given in water masked with a few drops of menthol, so that the patients thought they were taking a medicament. This medication was continued for several days except in instances in which there was an immediate positive reaction.

These results show that except in one case of chronic eczema the symptoms markedly increased, at any rate after several days' adminis-

TABLE 1.—*Data on the Reactions of Patients Given 20 Gm. of Sodium Chloride Daily for Several Days*

	Positive Reactions Appearing Each Day							
	First Day	Second Day	Third Day	Fourth Day	Fifth Day	Sixth Day	No Reaction	Number of Patients
Urticaria	10	4	—	1	2	1	—	18
Chronic eczema	4	6	4	5	—	—	1	20
Acute eczema	6	5	1	—	—	—	—	12
Neurodermatitis	10	2	2	—	2	—	—	16
Dyshidrosis	2	2	—	1	1	—	—	6
Total	32	19	7	7	5	1	1	72

tration of sodium chloride. In most cases the exacerbation was so striking that the patient experienced considerable shock, and the administration of sodium chloride had to be promptly discontinued. The medication aggravated the itching in particular, until it became unbearable.

This caused us to inquire which component of sodium chloride—cation, chloride or whole molecule—governs the noxious action. An accidental observation clarified this point. In a case of urticaria in which injections of solution of sodium chloride were made as controls for tuberculin tests, each intracutaneous injection of the solution produced local wheals. Wheals were produced also by the administration of isotonic solutions of other sodium salts (sodium sulphate and sodium carbonate) but not by control injections of isotonic solution of dextrose or by injections of a solution of calcium chloride, magnesium chloride or potassium chloride. Further tests on twenty-six patients with urti-

caria gave the same result in twelve instances. The data on the experiments with various salts are as follows:

TABLE 2.—*Data on the Results of the Administration of Isotonic Solutions of Sodium Chloride and of the Control Injections of Isotonic Solutions of Dextrose, of Chlorides Other than Sodium Chloride and of Sodium Sulphate and Sodium Carbonate*

Isotonic Solution	Number of Cases											
	1	2	3	4	5	6	7	8	9	10	11	12
Sodium chloride	2*	2	2	3	2	2	2	1	3	3	3	2
Potassium chloride	—	—	—	—	—	—	—	—	—	2	—	1
Calcium chloride	—	—	—	—	—	1	—	1	—	—	—	—
Magnesium chloride	—	1	—	—	—	—	—	—	—	—	—	—
Dextrose	—	—	—	—	—	—	—	—	—	—	—	—
Strontium chloride	—	—	—	—	—	—	1	—	—	—	—	—
Sodium carbonate	1	2	3	2	3	2	2	2	2	3	2	3
Sodium sulphate	1	2	2	3	3	2	1	3	3	2	2	2
Lithium chloride	2	2	2	3	2	2	2	1	3	3	3	2

* The figure 1 means +; 2, ++; 3, +++; —, negative.

This series of experiments showed that the irritative action of sodium chloride is due to the sodium. All sodium salts caused this reaction, whereas the chlorides of other metals, except lithium chloride, produced no wheals. The reaction from the administration of lithium chloride was equivalent to that obtained with sodium chloride.

That oral administration of sodium chloride should give the same reaction was to be expected in view of the fact that the chlorides of potassium, calcium and magnesium have a favorable influence on diverse dermatoses. But, in addition, we gave sodium carbonate to a group of ten patients in a daily dosage of from 20 to 25 Gm., which caused considerable exacerbation of cutaneous symptoms. These results correspond with the known action of sodium chloride in the pathologic process of edema, which is governed by the sodium cation (L. Blum, Magnus-Levy, etc.) but immediately raise the question of why the large amounts of sodium which are contained in the fluids of the body should be harmless. This question is related to the clarifying research of American authors (J. Loeb and Gellhorn) and German authors (Hoeber and Schade) on the physiologic effects of salts. It is true that experiments on the ionic antagonism and the mutual compensation of the action of the cations have so far not been extended to clinical medicine.

The results of experiments on this subject caused us to consider whether it is possible to compensate the observed reactions to sodium chloride by adding other salts, viz., so-called sodium antagonists, to sodium chloride. We therefore first tested, empirically, different combinations of salts. We found that definite quantitative relations of the chlorides of sodium, potassium, calcium and magnesium failed to pro-

duce any positive reactions, even when the mixture contained the same amount of sodium chloride which had previously produced wheals without the admixture of other salts.

We then gave this mixture of salts by mouth in doses which contained the same amount of sodium as the previously employed provocative doses of sodium chloride. Despite its high sodium chloride content, the mixture of salts never caused the exacerbation of pathologic symptoms which we observed in the other experiments; indeed, under its exclusive and prolonged use dermatoses improved or even were cured. In reality it is not surprising that the "detoxicated" mixture of salts, the composition of which we arrived at by the methods described, has approximately the same relative cation proportions as the cation relation of the blood fluid and the largely identical and significant cation relation of sea water. These results yield the following conclusions:

The action of sodium chloride on the skin is due to the cation component and causes exacerbation of cutaneous symptoms. This action depends on a disturbance of the equilibrium between sodium and the other cations in the body. If sodium is given not by itself but equilibrated with potassium, calcium and magnesium salts, it does not exacerbate the pathologic symptoms. When the customary salt-rich diet has disturbed the cation equilibrium previously, this disturbance is corrected by administration of the equilibrated mixture of salts, resulting in the cure of those pathologic processes which were maintained by the preexistent disturbance of the mineral economy. The following additional experiments furnished further proof and indicated the therapeutic utilization of the results.

1. The customary salted diet causes excessive enrichment of the sodium content at the expense of the amounts of potassium, calcium and magnesium in the body. This is demonstrable chemically. Considerable fluctuations of the cation relations are possible within the normal limits of the cation relation of the blood serum. For instance, sodium may lie in the upper, and potassium, calcium and magnesium in the lower, limits of the milligram values per hundred cubic centimeters. Hence it is much more important to investigate the mutual relation of the individual cations than their absolute values. It is useful not to consider the relative values in grams per hundred cubic centimeters but to calculate the equivalents of the individual cations. This prevents the different atomic weights from obscuring the actually decisive quantitative proportions. Unfortunately the literature is so far entirely lacking in such reports of comparative values.

The many hundreds of observations which we have made show that the fluctuations of the cation relation, expressed in equivalents, with

sodium as 100 mols are: for potassium, from 2.57 to 5 mols; for calcium, from 1.2 to 2.5, and for magnesium, from 1.4 to 6. But these limits of the relation between sodium and the individual cations are not utilized by the organism simultaneously for all the cations. On the contrary, as a rule, when an increase of potassium takes place, it is attended by a certain diminution of calcium and of magnesium, and conversely. The values which are decisive for the composition of the blood and are fixed within the narrowest limits are obtained by considering on the one hand sodium and on the other, collectively, the cations which antagonize sodium, viz., potassium, calcium and magnesium. Our material then showed fluctuations in the sum of the three antagonistic cations varying between 5 and 9 mols, on the basis of a value for sodium of 100 mols. The value of sodium when potassium plus calcium plus magnesium equals 7 mols or over should

TABLE 3.—*Data on the Effects of Excessive Enrichment of the Sodium Content on the Potassium, Calcium and Magnesium Content of the Blood Serum*

Patient	Diet	Date	Sodium, Mg. per 100 Cc.	Potassium, Mg. per 100 Cc.	Calcium, Mg. per 100 Cc.	Magnesium, Mg. per 100 Cc.	Mols of Potassium, Calcium and Magnesium per 100 Mols Sodium
Schmidt.....	From 9/8, salt-free	9/30	414.00	21.09	11.61	2.79	5.17
		10/ 9	341.55	21.50	12.14	2.35	6.26
		10/19	303.60	21.97	12.14	6.99	8.64
Baum.....	From 10/16, equilibrated salt	10/16	381.80	26.84	12.38	3.27	6.60
		10/21	343.85	32.25	11.80	3.45	8.38
Bieberitz.....	Four days salt-free	10/ 7	339.25	29.88	12.09	2.95	8.00
	Eight days, sodium chloride	10/22	489.90	25.69	11.80	2.54	4.88
		10/14	385.75	24.20	12.95	3.10	6.27
Timm.....	Twenty-six days, salt-free	10/26	327.75	29.40	12.85	3.45	8.55
		10/16	339.25	26.70	12.28	2.35	7.26
Koch.....	Eight days, salt-free	10/23	362.25	26.03	12.85	7.45	8.16

correspond to the normal value after sufficiently prolonged administration of a salt-free diet. According to our research lesser values for antagonists than these indicate the presence of pathologic processes and are a manifestation of the continuous intake of sodium chloride with the food. The marked chemicophysical effect of such deviations in the cation relation on the sensitive cell protoplasm renders understandable the production of pathologic reactions. The relation of the salts in the interior of a cell is subject to far greater fluctuation, but the process of demineralization is perfectly demonstrable in the blood fluid.

The disturbance of the cation relation can be compensated by means of a salt-free diet, by a diet in which equilibrated salt is used or by an increased intake of potassium, calcium and magnesium salts. This regression of the excess of sodium precedes, or runs parallel to, the cure of the clinical symptoms.

2. The alteration of the intake of mineral salts causes no direct injury to the skin but increases the responsivity to stimuli. To prove this fact experimentally, sixty patients were examined for erythema due to irradiation with an air-cooled quartz mercury vapor arc lamp. This experiment was carried out in conjunction with Papcke between November 1931 and February 1932, which excluded possible disturbing alterations of the erythema capacity of the skin by climatic influences in the spring. With the aid of a Boehmer erythema tester ten rectangular fields on one thigh were irradiated for from one to ten minutes. The resulting erythema was examined twenty-four hours later and its intensity appraised. For the following fourteen days the patient then received, three times daily, from 1 to 2 Gm. of an isotonic mixture of potassium, calcium and magnesium salts. Following this the precise corresponding part on the other thigh was irradiated as

TABLE 4.—*Data on the Favorable Therapeutic Results Obtained by the Replacement of Pure Sodium Chloride with the Equilibrated Mixture of Salts in the Diets of Ambulatory Patients*

Diagnosis	Number of Patients	Uninfluenced	Slightly Improved	Markedly Improved	Cured
Psoriasis vulgaris	15	13	—	2	—†
Pemphigus vulgaris	7	7	—	2	—
Lichen ruber planus	27	—	—	3	24‡
Dermatitis herpetiformis	12	1	—	2	9
Urticaria	90	3	—	13	74
Eczema	841	38	62	429	312
Arsphenamine dermatitis	27	—	3	6	18§
Toxic exanthem	18	—	—	—	18
Secretory and circulatory anomalies*	342	12	21	216	94‖
Neurodermatitis	68	1	—	16	51
Tuberculosis of the skin	38	—	3	15	20¶

* Hyperhidrosis, seborrhea, acne vulgaris, rosacea and acro-asphyxia were included.
† Psoriasis proved wholly refractory and was therefore not included in the further experiments, although in two cases considerable itching was greatly improved by the diet.
‡ Among these were patients with lichen ruber pemphigoides.
§ The curative course was shortened distinctly.
‖ These patients had hyperhidrosis, acne vulgaris and seborrhea rosacea.
¶ The diet does not act directly on the tubercle bacilli but merely increases the local tissue resistance and in this way indirectly leads to the cure of the pathologic process.

before. On comparing the two readings fourteen days later, of sixty cases the inflammatory capacity was diminished in fifty-two (86.67 per cent), unchanged in two (2.33 per cent) and slightly increased in six (10 per cent). In control experiments it was found that with the same diet for the same period the erythema capacity did not alter, whereas it increased suddenly following increased intake of sodium chloride.

3. The exclusion of pure sodium chloride and its replacement by the equilibrated mixture of salts yielded surprisingly favorable therapeutic results. The statistics in table 4 enumerate only the results on ambulatory patients. Patients confined to bed, of course, show considerably better results, as the diet can be carried through better and more easily

with them. Altogether about fifteen hundred ambulatory patients with cutaneous diseases were treated dietetically by us. We took care that the diet was adequately rich in all vitamins, but apart from this we simply prohibited the use of sodium chloride strictly and replaced it by equilibrated salt.

These experiments show the considerable importance of mineral economy to the skin and to its diseases. The decisive factor in the actions of the mineral salts falls to the cations and their reciprocal quantitative proportions. That clarifies at the same time the manner of action of a salt-free diet. Obviously the decisive factors are the electrophysical influences of the cations on the colloids of the cells, and the alterations of the reactive state of the organs which are connected therewith. This, however, yields an extension of the indications of dietary therapy to internal diseases, with a salt the cation content of which is equilibrated, so far as they represent functional anomalies (vegetative disturbances). The mineral economy can be influenced and regulated by various forms of a salt-free diet, among which is the Gerson-Herrmannsdorfer-Sauerbruch diet. This diet is, however, difficult to carry through for lengthy periods owing to its unpalatability. The manner of action of sodium chloride having been elucidated, it would seem more useful to give a diet with equilibrated salt instead of a salt-free diet or, in instances in which this should prove impracticable, to prescribe the addition of potassium, calcium and magnesium salts to the customary food.

EPITROCHLEAR ADENOPATHY IN SECONDARY SYPHILIS

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The importance of epitrochlear adenopathy has given rise to considerable discussion. Some believe it to be of prime importance, while others think that it is of little or no value. I have examined 100 patients with secondary syphilis and am adding the observations to the literature, which is by no means bulky. This constitutes the raison d'être for this paper.

REVIEW OF THE LITERATURE

Delamère,[1] in an exhaustive study of the lymphatic glands, said that two epitrochlear glands are not uncommonly present on the same side and that even three may be present. Gray's "Anatomy" states the same opinion. Queyrat [2] saw a patient with five epitrochlear glands on the left side and two on the right. The person had contracted syphilis four months previously. In Queyrat's experience the presence of four such glands on one side is not uncommon; he observed it on several occasions. An involved epitrochlear gland often assumes the size of a pea, but it may attain the dimensions of a navy-bean and exceptionally those of a small olive. It is well to remember that it may lie several centimeters above its customary site.

Auzeloux credited Sigmund [3] with first calling attention to the importance of epitrochlear adenitis in syphilis. Unfortunately, I was unable to consult his original article. Campana [4] found such glandular involvement in only 2 of 20 patients with secondary syphilis. In his book devoted largely to syphilis in women Fournier [5] said that the importance of epitrochlear adenopathy had been greatly exaggerated, since in an examination of several hundred syphilitic patients he found only a few

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1. Delamère, G.: General Anatomy of the Lymphatics, in Poirier, P., and Cunéo, B.: Anatomy, translated by Cecil H. Leaf, London, Constable & Co., Ltd., 1913, p. 234.

2. Queyrat: Deux cas d'adénopathie épitrochléenne rare, Bull. Soc. franç. de dermat. et syph. **14**:74 (Feb.) 1903.

3. Sigmund, quoted by Auzeloux.[13]

4. Campana, Roberto: Delle limfadenopatie sifilitiche: Studi clinici, Gior. ital. d. mal. ven. **6**:2 and 94, 1872-1873.

5. Fournier, A.: Leçons clinique sur la syphilis etudiée plus particulièrement chez la femme, Paris, Delahaye et Lecrosnier, 1881, p. 474.

cases. Later Fournier [6] conceded that the finding of this condition might be of diagnostic value, and he quoted de Amicis, who found it in 25 per cent of the patients with secondary syphilis whom he saw.

Of 2,119 cases of syphilis de Amicis [7] found involvement of the epitrochlear gland in 480. These were from his clinic in Naples. Among 100 patients with syphilis seen in private practice only 13 failed to show a similar adenitis. De Amicis, as quoted by Auzeloux, spoke of epitrochlear adenopathy as being the pulse of syphilis. He concluded that it is one of the most frequent manifestations of that disorder, that its absence may be due to a physiologic absence of the gland itself, that it may persist long after other glandular enlargements have disappeared, and that when local causes for such adenopathy can be eliminated it is a valuable sign of syphilis, particularly in doubtful cases.

Batut [8] stated the belief that the presence of epitrochlear adenopathy is a reason for suspecting syphilis in a given patient, but since he has frequently observed it in tuberculosis, it should not be regarded as absolutely characteristic.

Fernet [9] deplored the lack of interest in enlargement of the lymph glands. In his opinion epitrochlear adenitis is of real value from the retrospective standpoint because of its lengthy duration.

Friedlander [10] studied glandular enlargement on 100 patients with syphilis, with reference to the epitrochlear, occipital and posterior cervical glands. All of the patients presented characteristic cutaneous lesions plus positive serologic findings. Among the patients in whom syphilis had lasted less than one year Friedlander found unilateral epitrochlear adenitis in 93.50 per cent and bilateral involvement in 85.50 per cent. Patients with syphilis lasting from one to two years had an incidence of unilateral epitrochlear adenitis of 93 per cent and of bilateral involvement of 78.50 per cent. In those who had contracted syphilis from two to three years previously, the respective incidence of epitrochlear adenitis was: unilateral, 82.50 per cent, and bilateral, 75 per cent. Among 100 patients with conditions classed as nonsyphilitic Friedlander found unilateral epitrochlear adenopathy in 42.50 per cent and bilateral adenopathy in 27.50 per cent. In his experience the occipital and posterior cervical glands were less frequently involved in patients with syphilis.

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6. Fournier, A.: Traité de la syphilis, Paris, J. Rueff et Cie, 1906, vol. 1, p. 546.

7. de Amicis, quoted by Auzeloux.[18]

8. Batut, L.: Des adénopathies non chirurgicales, J. d. mal. cutan. et syph. **20**:321, 1909.

9. Fernet, C.: Des adénopathies en général et de leur valeur diagnostique, J. de méd. et chir. prat. **88**:161, 1917.

10. Friedlander, D.: The Value of Lymphatic Gland Examination in the Diagnosis of Syphilis, J. Cutan. Dis. **30**:14, 1912.

Lévy-Franckel [11] stated the belief in the importance of epitrochlear adenopathy in syphilis. He found it to be conspicuously absent in glandular and pulmonary tuberculosis as well as in lupus vulgaris in a large number of patients, both children and adults, whom he studied at the Hôpital Saint-Louis. He found this form of adenitis to be frequent in latent syphilis but inconstant in florid syphilis. Lévy-Franckel cited 10 instances of untreated secondary syphilis in which such adenopathy led to a diagnosis of syphilis, which received serologic confirmation in all instances.

Rulison,[12] who made a most interesting contribution to this subject, may be quoted in part as follows:

> Anatomists agree that the epitrochlear gland is inconstant. In the absence of definite figures perhaps it is justifiable to take those collected from cases of secondary syphilis in this series and to say that the gland is probably absent, rudimentary or misplaced on both sides in from 10 to 14 per cent of individuals; that it is unilateral in from 14 to 20 per cent and that it is bilaterally present and sufficiently developed to be palpable when enlarged in from 72 to 75 per cent of individuals. In probably 3 per cent of individuals the glands on one or both sides are multiple, usually two but as many as five having been palpated. The frequently expressed opinion that unilateral epitrochlear enlargement is of less diagnostic importance than bilateral does not seem to be well founded.

In only 12 of 94 men with secondary syphilis did Rulison fail to find enlarged epitrochlear glands. Bilateral epitrochlear adenopathy was present in 68 of his patients. The adenitis was unilateral in 14. It is his belief that epitrochlear adenopathy is an early, persistent and common sign of syphilitic infection. It is not pathognomonic, for it may appear in nonsyphilitic persons, but it is a valuable diagnostic aid, especially in cases of latent and treated syphilis.

Auzeloux [13] studied 82 cases of secondary syphilis in the service of Sézary at the Hôpital Saint-Louis. All of them presented characteristic cutaneous or mucosal lesions plus positive serologic reactions. Epitrochlear adenopathy was present in 39 of them, being unilateral in only 7. Auzeloux stated the belief that while this form of adenitis is not pathognomonic of syphilis its presence strongly suggests that disorder. It was very persistent in his patients.

Musser [14] said: "Enlarged epitrochlear glands usually indicate syphilis, active or latent."

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11. Lévy-Franckel: Les adénopathies sus-épitrochléennes dans la syphilis, Ann. d. mal. vén. **9**:508 (July) 1914.

12. Rulison, R. H.: Epitrochlear Adenopathy in Syphilis, Am. J. Syph. **5**:643 (Oct.) 1921.

13. Auzeloux, Jean: Contribution à l'étude de l'adénopathie épitrochléenne au cours de la syphilis secondaire, Thèse de Paris, no. 119, Paris, Jouve & Cie, 1931.

14. Musser, J. H.: Practical Medical Treatise on Medical Diagnosis, ed. 6, Philadelphia, Lea & Febiger, 1913, p. 144.

Keyes [15] expressed the opinion that when both the epitrochlear and the posterior cervical glands are enlarged such a combination is almost diagnostic of syphilis.

Stokes [16] said: "The epitrochlear enlargement when marked and symmetric has high suggestive value."

One hundred patients with secondary syphilis were examined for evidence of epitrochlear adenopathy. Without exception they presented characteristic lesions of the skin or mucous membrane, sometimes of both, plus positive serologic findings. Their ages ranged from 17 to 65 years. Forty-two per cent were men, and 35 per cent were Negroes. Bilateral epitrochlear involvement was found in 27 patients, 11 of whom were Negroes. In 13 patients the epitrochlear adenopathy was unilateral, with the right epitrochlear gland involved in all but 2 instances. In none of these cases could a local cause be held responsible for the adenitis, nor was there any evidence of Hodgkin's disease or leukemia. There were 2 examples of multiple involvement of epitrochlear glands.

A Negro (case 4) presented two enlarged epitrochlear glands on the left side and four on the right side, while another patient (case 52) had two such glands on the right side and one on the left. Both patients showed a maculopapular exanthem. Bilateral epitrochlear adenopathy was associated with rupioid syphilis in 2 patients (cases 46 and 53). One patient (case 66) had typical rupioid syphilis with unilateral adenitis, while 3 patients (cases 41, 45 and 78) presented typical examples of *syphilis maligne précoce* with no evidence of epitrochlear adenopathy.

CONCLUSIONS

Epitrochlear adenopathy occurs often enough in syphilis to be of value as a diagnostic sign, particularly when it is bilateral. It was found in 27 of 100 patients.

Epitrochlear adenopathy may be present or absent in severe cases of syphilis.

Such adenitis may appear in nonsyphilitic persons, but when not due to a local cause a careful search should be made for other evidence of syphilis.

30 North Michigan Boulevard.

15. Keyes, E. L.: Syphilis, New York, D. Appleton & Company, 1908, p. 263.

16. Stokes, J. H.: Modern Clinical Syphilology, ed. 2, Philadelphia, W. B. Saunders Company, 1934, p. 688.

NONFATAL JAUNDICE ASSOCIATED WITH ARSPHENAMINE THERAPY

CLINICOPATHOLOGIC STUDY OF TWO CASES

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Not infrequently during or after arsphenamine therapy, visible jaundice develops rather suddenly in certain patients and within from a few days to several weeks terminates in clinical recovery. Because of the benign course of this jaundice, material for gross and histologic examination is practically unavailable. Most discussions, therefore, dealing with the etiology and morbid anatomy of the condition have been characterized by inferences drawn from clinical observations rather than by conclusions founded on pathologic data.

We report the following two cases of nonfatal jaundice associated chronologically with arsphenamine therapy because in each instance we had the unusual opportunity of making adequate histologic studies of the liver. In case 1 the patient died from a bleeding peptic ulcer and ascending pyelonephritis four weeks after jaundice had disappeared from the skin and scleras. In case 2 material for biopsy of the liver was obtained during the height of icterus at laparotomy performed for suspected cholelithiasis.

REPORT OF CASES

CASE 1.—*History and Course.*—F. S., an unmarried man, aged 39, a painter, was admitted to the Buffalo General Hospital on Dec. 14, 1932, complaining of jaundice of seven days' duration.

About six months before he had consulted a physician because of diplopia, weakness in the legs and urinary incontinence. These symptoms had progressed steadily for two years. The patient also complained of a burning pain in the epigastrium, which was relieved by vomiting. Physical examination revealed that the pupils were irregular and unequal and did not react to light. The deep reflexes were absent. Laboratory studies disclosed a strongly positive Wassermann reaction of the blood and spinal fluid; the albumin and the globulin content were each 1+. The clinical impression was tabes dorsalis.

This paper is dedicated to Prof. Anton Ghon, Prague, Czecho-Slovakia, in honor of his seventieth birthday.

From the Pathological Laboratory, K. Terplan, M.D., Director, and the Department of Dermatology and Syphilology, Earl D. Osborne, M.D., Director, the Buffalo General Hospital, and the University of Buffalo Medical School.

The patient received 0.4 Gm. of arsphenamine intravenously on July 27 and on Aug. 3, 1932. A severe reaction with fleeting jaundice is said to have followed the second dose. On August 10 and 17, 0.3 Gm. of silver arsphenamine was given in split doses. Transient jaundice again appeared. Sodium thiosulphate (1 Gm.) was administered. The administration of silver arsphenamine in split doses (0.3 Gm.) was continued for three weeks. Jaundice did not recur. Fifteen doses of bismuth salicylate (0.13 Gm. each) were administered from Sept. 21 to Dec. 7, 1932.

Acute jaundice developed on Dec. 7, 1932, and became more intense during the next week. On the patient's admission the skin and scleras were distinctly icteric. The liver was palpable 2 fingerbreadths below the costal margin and was smooth. While the patient was under observation he complained of epigastric pain and nausea. He also had difficulty in voiding. The temperature ranged from 100 to 102 F. About one week after admission the liver could not be palpated. Up to that time the patient had received 4 Gm. of sodium thiosulphate intravenously and 2 Gm. orally. On December 22 the icterus was fading; in the next week it had entirely disappeared from the skin and scleras. On Jan. 10, 1933, the patient suddenly vomited 1,500 cc. of blood. Despite supportive treatment he became weaker, continued to vomit blood and had fever. Jaundice did not reappear. Death occurred on January 28.

Laboratory Examination.—On Dec. 15, 1932, the bile content of the urine was 2+; on December 24 the test was negative. On December 17 the test for urobilinogen was positive; examination of the stool showed bile; the van den Bergh reaction was positive and immediate and showed 25 units of bilirubin. On December 28 the van den Bergh test was negative, showing less than 0.6 units of bilirubin. On December 17 the bromsulphalein test showed 100 per cent retention after thirty minutes, and on Jan. 3, 1933, it showed 20 per cent retention after thirty minutes. The results of other tests on January 3 were as follows: phenolsulphonthalein test, 20 per cent excretion after two hours; sugar content 98 mg., urea nitrogen 15 mg. and calcium 8 mg. per hundred cubic centimeters of blood; duodenal drainage gave negative results for cholesterol crystals, leukocytes and pathogenic bacteria; tests for arsenic in the urine showed from 16 to 20 mg. in twenty-four hours. Roentgen examination showed an elevation on the lesser curvature in the midportion of the stomach; this was interpreted as an ulcer. A five hour residue was present.

Postmortem Examination.—The autopsy was performed fifty-three hours after death. The brain and spinal cord were not dissected because of restrictions. The chief anatomic changes comprised: a chronic, peptic ulcer the size of a quarter on the lesser curvature of the stomach with erosion of three small arteries in its base; gastro-enterorrhagia; generalized anemia; diffuse purulent hemorrhagic cystitis with trabeculation of mucosa; bilateral pyo-ureter and pyelonephritis; syphilitic meso-aortitis; moderate smooth atrophy of the liver; fibrous perihepatitis of the anterior surface of the right lobe with adhesions to the diaphragm.

Macroscopic Appearance of the Liver: The liver appeared small; it weighed 1,000 Gm. The right lobe measured 16 by 16 by 6.3 cm.; the left lobe, 13 by 6 by 3 cm. The greatest diminution in size was noted in the left lobe. The inferior border, especially that of the left lobe, was sharp. The surface was smooth. Dense fibrous adhesions, however, ran from the anterior surface of the right lobe to the diaphragm. The consistency was fairly normal. On section the color was pale. The markings appeared obvious. The lobules were small. In the right

lobe there was a dime-sized circular grayish-red area showing no lobular structures. The gallbladder was thin-walled and contained about 20 cc. of greenish bile. The mucosa was intact. There were no stones. The bile ducts were thin-walled and patent, and their circumference was normal. The bile was normal. The ampulla of Vater was patent. The spleen was not enlarged.

Microscopic Appearance of the Liver: Blocks of tissue were taken from both lobes and fixed in a 10 per cent solution of formaldehyde and alcohol. Frozen sections were stained with hematoxylin and eosin and sudan III. The Van Gieson, Turnbull blue, and silver impregnation stains (Foot and Foot variant 2) were used on paraffin sections. The Levaditi, Gram-Weigert, and methylthionine chloride (U. S. P.) stains were also used.

In the gray patch noted grossly no parenchymal structure remained. The patch was made up of rather compact fibrous tissue. Most of the fibers were impregnated with the silver stain. The fibrous patch also took a slight pink stain with the Van Gieson method. A few capillaries were dilated with red blood cells. There was a distinct round cell infiltration. Especially outstanding was the marked proliferation of bile ducts. Because of their great numbers the histologic picture almost resembled that of a malignant tumor. Surrounding the fibrous patch were many small nodules of hepatic cells which possessed no lobular structures. These cells showed degenerative changes in their cytoplasm.

Outside of the gray patch just described the hepatic architecture appeared well preserved. The lobules, however, were smaller than normal. In practically every lobule a striking pathologic change was noted in the central zone. The lesion continued from one central zone to another. The central veins were slightly dilated; they contained almost no red blood cells. Their walls were perhaps slightly thickened. The architecture of the liver cords about the central veins was destroyed in fully from one fourth to three eighths of each lobule. In this area the hepatic cells had almost completely disappeared. Only here and there was a single cell or syncytial mass scattered. In these masses the outlines of the cells were indistinct; their shapes were shrunken and distorted. The cytoplasm took a pale stain; it was loaded with yellowish-green granules and huge vacuoles. The nuclei were fragmented and pyknotic. In some cells no nuclei were seen. The reticulum in the central zone was collapsed and thickened. A regular sinusoid structure could not be made out. Dispersed throughout was cytoplasmic and nuclear débris. Greenish glistening structures, round and needle-shaped, could be seen. In a few lobules the sinusoids were still dilated with red blood cells; there was an infiltration of polymorphonuclear leukocytes, eosinophils and round cells; macrophages with greenish pigment were in evidence.

In the liver cords adjacent to the central zone regressive changes were prominent. Cells showed granules and vacuoles in their cytoplasm. The nuclei were swollen, pale and eccentric. Sections stained with sudan III exhibited distinct fatty degeneration. The cells in the middle and peripheral zones were well preserved. They appeared, however, somewhat small and shrunken from the reticulum; sinusoids were prominent. In patches, especially near the portobiliary spaces, isolated cells and clusters of cells showed degenerative changes and necrosis. Cells with double nuclei were also present. The sinusoids contained many leukocytes. The portobiliary spaces adjacent to these focal areas of regressive changes contained a moderate number of leukocytes and round cells. Otherwise, the portobiliary spaces seemed prominent; there was a distinct fibrosis; inflammatory reaction was negligible; the bile ducts were patent and slightly increased in number. Neither spirochetes nor bacteria were found.

CASE 2.—*History and Course.*—A. L., a housewife aged 36, was admitted to the Buffalo General Hospital on April 18, 1932, complaining of jaundice of one week's duration. She was discharged as improved on July 13, 1932.

During the course of an examination in April 1931 a Kahn test was reported as positive. (On six previous admissions for surgical and obstetric treatment Wassermann tests had been negative.) From April 30 to Sept. 17, 1931, fifteen

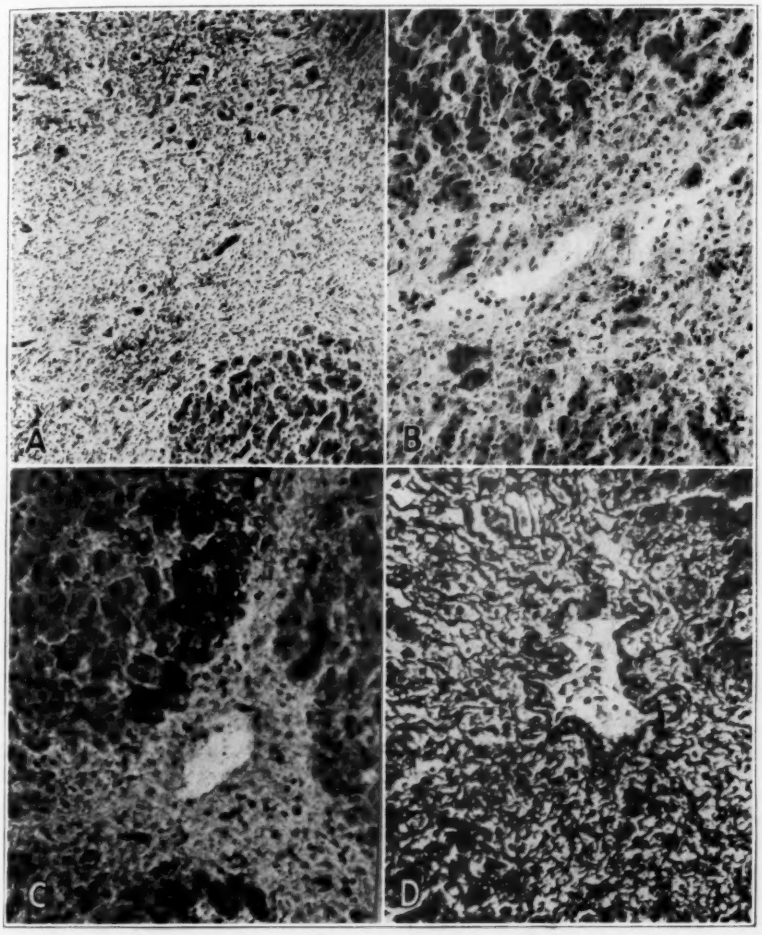

Fig. 1.—*A*, section of gray nodule noted grossly showing loss of hepatic lobules, fibrous tissue, proliferating bile ducts and peripheral nodules of hepatic cells as seen under low magnification; *B*, disappearance of hepatic cells in the central zone and a small number of remaining degenerated and necrotic cells as seen under medium magnification; *C*, fatty degeneration in hepatic cords adjacent to the central zone as seen under medium magnification; *D*, collapse of reticulum in the central zone as seen under medium magnification.

injections of bismuth salicylate, of 0.13 Gm. each, were given in the buttock. On October 2 the patient received 0.2 Gm. of arsphenamine intravenously, and on

October 8 and October 22 she received the same dose. After the last treatment she failed to return to her physician for further therapy.

On admission to the hospital, on April 18, 1932, the patient claimed that she had been "perfectly" well until two weeks previously, when she began to suffer with anorexia, nausea and emesis. There was no abdominal pain. One week later the skin became yellow, and the stools were clay-colored. No history of ingestion of drugs or of jaundice in the family or in the neighborhood was obtained.

The temperature was 99 F. The skin and scleras were jaundiced. The pupils reacted to light and in accommodation. The liver was distinctly palpable and tender. The reflexes were normal. On May 12 the patient complained of severe pain in the right upper abdominal quadrant; the pain radiated to the back and necessitated administration of morphine. Laparotomy for suspected cholelithiasis was performed on May 29. The liver and spleen were enlarged; adhesions were

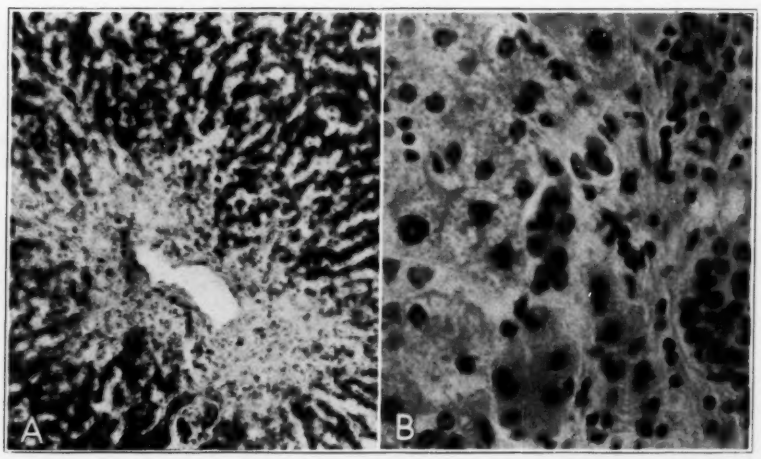

Fig. 2.—Sections from a hepatic lobule. *A* shows disappearance of cells in the central zone and prominent portobiliary space as seen under low magnification. *B* shows a focal area in the periphery of the lobule presenting cellular degeneration and necrosis and slight cellular infiltration in the adjacent portobiliary space as seen under high magnification.

found between the liver and the diaphragm. The stomach, duodenum and pancreas appeared normal. The gallbladder emptied freely. No calculi were palpated. The common duct was not dilated. Material for biopsy was taken from the right lobe of the liver. By June 9 the jaundice had definitely diminished. Three weeks later the liver was not palpable. On July 13 the jaundice was invisible in the skin and scleras.

Laboratory Examination.—The blood count showed from 6,600 to 8,000 white cells with 61 per cent neutrophils, 37 per cent lymphocytes, and 2 per cent eosinophils; the Kahn test was negative; the urine contained bile on admission, but the test was negative on June 13. The test for urobilinogen was positive on April 9 and negative on April 30. The stools contained bile on admission, but showed a negative reaction on April 30. The blood sugar content was 112 mg.

per hundred cubic centimeters; the urea nitrogen content was 12 mg.; the cholesterol content, 125 mg., and the calcium content, 8.8 mg.; the van den Bergh reaction was positive, direct and immediate, showing 40.9 units on April 18, 62.7 units on May 10 and 6 units on June 12. The bromsulphalein test showed 100 per cent retention after thirty minutes; the phenolsulphonphthalein test showed 81 per cent excretion in two hours on April 22 and 65 per cent excretion on June 14. Tests for

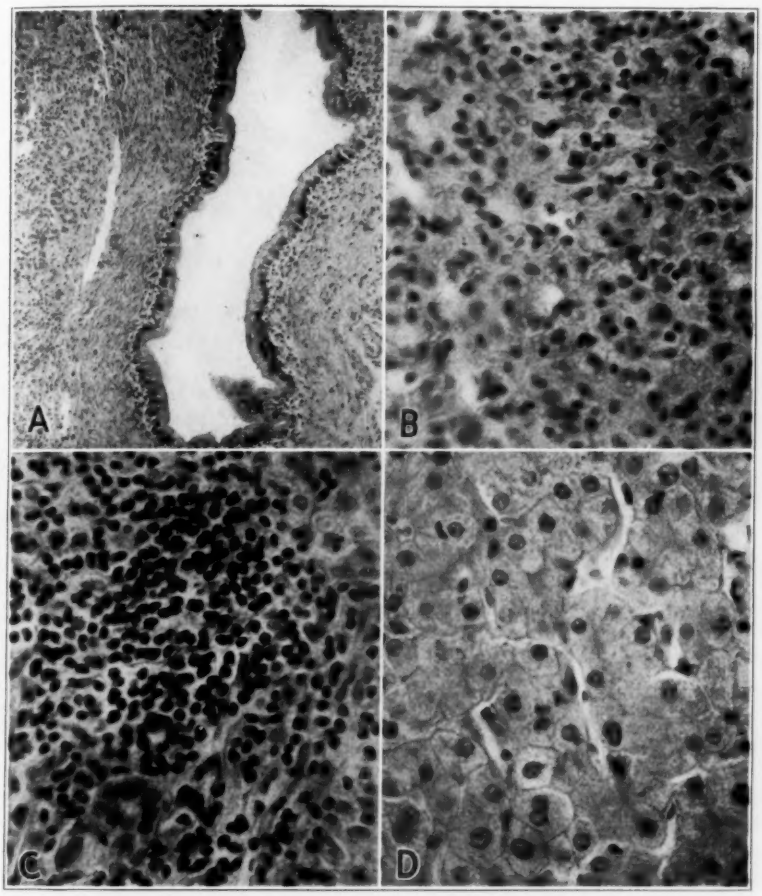

Fig. 3.—*A*, larger bile duct showing patent lumen, intact mucosa and walls free from inflammation as seen under low magnification; *B*, loss of hepatic cells, swelling of endothelial cells and dilatation of sinusoids with red blood cells as seen under high magnification; *C*, portobiliary space, showing increase in bile ducts and capillaries, infiltration with leukocytes and round cells and proliferating fibroblasts as seen under high magnification. *D*, section showing preserved hepatic cells presenting degenerative changes and necrosis, cells with double nuclei, and compression of sinusoids as seen under high magnification.

galactose performed after the operation gave the following results: A control test was negative; after four hours one sample contained 3.5 Gm. Duodenal drainage

gave negative results for cholesterol crystals, leukocytes and pathogenic bacteria; the amount of arsenic in the urine was 12 mg. per thousand cubic centimeters.

When the patient was seen six months after her discharge from the hospital she had no complaints. Transient jaundice, however, had reappeared on two occasions for one day in connection with gastric distress. The liver was not palpable. The bromsulphalein test showed no retention; the van den Bergh reaction showed 1.5 units.

Pathologic Examination.—The excised piece of liver measured 1 by 0.8 by 0.3 cm. Except for one small area in the inner part, the tissue was depressed and red; normal markings could not be seen. Microscopic examination revealed that in the major portion of the specimen, especially in the outer half close to the capsule, the normal parenchymal structure had disappeared completely. The lobular boundaries were partially collapsed. In the portobiliary spaces, which were fairly recognizable, the small bile ducts and capillaries seemed distinctly increased in number. Surrounding them was a dense infiltration of polymorphonuclear leukocytes, round cells and occasional plasma and eosinophil cells. There were also large oval cells possessing pale spindle-shaped nuclei—apparently proliferating fibroblasts. The small bile ducts were patent. They contained no bile thrombi or exudate. The remainder of the lobules was made up of markedly dilated sinusoids filled with erythrocytes. The endothelial cells were swollen. Hepatic parenchymal cells could not be distinguished. Only occasionally degenerated and necrotic cells with greenish pigment and globules in their cytoplasm could be seen. Scattered throughout were cells of inflammatory origin. The entire picture in this outer collapsed region of the biopsy specimen resembled that of an older stage of red atrophy with unusually marked reactive inflammation and with prominent proliferation of small bile ducts. In the inner part of the specimen the parenchymal cellular structure was still preserved in the elevated area noted grossly. Lobular structures, however, were obscured. The hepatic cells manifested pronounced acute and subacute regressive changes. They were swollen; the sinusoids were compressed and devoid of blood. The cytoplasm stained pale; it showed many granules and vacuoles. In many of the cords the outlines of contiguous cells were indistinct. There was apparently a confluence of degenerated cells. The nuclei were for the most part round, swollen and pale. Their positions were often eccentric. In many, nucleoli were not obvious. Nuclear fragmentation and pyknosis were prevalent. Many cells showed no nuclei. In contrast, cells with two, three and four nuclei formed a striking feature. Various lobules demonstrated that the necrotic changes occurred earlier and to a greater degree in the central zone. In that zone necrotic cells were numerous and contained yellowish-green pigment. Besides there were scattered cellular and nuclear débris and moderate numbers of leukocytes and lymphocytes. Where destruction of hepatic tissue was less advanced the inflammatory reaction tended to be slight.

The larger bile ducts were patent. Their lumens contained no thrombi, exudate or desquamated epithelium. The mucosa was intact. Except for a few round cells and leukocytes in the wall no inflammatory reaction was noted. Bacteria were not demonstrated.

COMMENT ON CLINICAL FINDINGS

In studying a case of jaundice which has appeared during or following arsphenamine therapy, clinicians recognize the theoretical possibility that the condition may be due to syphilis, to arsphenamine, to an intercurrent disease, such as toxic-infectious dystrophy of the liver (so-called

catarrhal jaundice), cholelithiasis, etc., or to a combination of any of these factors.

The initial jaundice in our case 1 seemed plausibly assignable to hepatic damage by arsphenamine. In the light of the frank evidences of syphilis which the patient presented and the inadequacy of previous therapy, late hepatic syphilis and a Herxheimer reaction, of course, could not be summarily disregarded as etiologic factors. Physical examination, however, revealed no signs of gummas or cirrhosis of the liver. The jaundice with which the patient had never before been afflicted developed in closest temporal relation to the injection of arsphenamine. Associated with its onset were other symptoms generally attributed to toxicity due to arsphenamine. Continuation of antisyphilitic therapy reproduced the jaundice instead of preventing its recurrence.

The etiologic diagnosis of the second attack of jaundice offered a difficult and complicated problem. Syphilitic hepatorecurrence was ruled out for reasons already given. In view of the absence of abdominal pain, the presence of bile in the feces and the negative results of duodenal drainage for crystals, leukocytes and pathogenic bacteria, obstructive jaundice due to calculus, cholangeitis, etc., was not seriously considered. Variations in size of the liver and alterations in the results of tests for hepatic function pointed forcibly to a primary intrahepatic lesion, most likely parenchymal and degenerative. As to the underlying cause of this lesion, opinions differed. Was the jaundice essentially the consequence of a delayed effect of arsphenamine which had been retained in the liver? Or was it solely a catarrhal type of jaundice precipitated by some unrecognizable toxic or infectious agent and modified only by the presence of syphilis and the history of arsphenamine therapy? Application of clinical criteria accepted by various observers to help answer these questions made the first probability, i. e., jaundice due to delayed effect of arsphenamine (per se), seem most attractive. But it must be stated that an explanation on the basis of a multiple etiology was also adduced. In other words, might not catarrhal jaundice develop more easily in a liver conditioned in some way by retained arsphenamine? Or might not arsphenamine exert a deleterious effect on hepatic cells suddenly made susceptible by an obscure toxic-infectious or metabolic factor?

The diagnostic possibilities which were considered in our second case included syphilitic hepatorecurrence, jaundice due to delayed effect of arsphenamine (per se), so-called catarrhal jaundice and cholelithiasis with obstruction of the common duct. Syphilitic hepatorecurrence was excluded when after complete examination it became evident that the patient could not be proved to be syphilitic. Even if she were suffering with latent syphilis the preliminary course of bismuth salicylate would

have protected her against hepatorecurrence. As in the first case, then, diagnosis resolved itself into differentiation between jaundice due to delayed effect of arsphenamine (per se) and catarrhal jaundice. In this patient, however, the clinical data (gastric prodrome, enlargement and tenderness of the liver, normal white cell count with slight relative lymphocytosis, small number of injections of arsphenamine received without untoward symptoms and length of time elapsing between treatment and onset of jaundice) favored the diagnosis of catarrhal jaundice. The progressive increase in icterus and the sudden appearance of severe abdominal pain radiating to the back and of acholic stools made the decision to operate for gallstones almost compulsory. The postoperative diagnosis reverted to catarrhal (intrahepatic) jaundice.

COMMENT ON PATHOLOGIC CHANGES

From gross examination alone gummas of the liver and syphilitic cirrhosis could be ruled out in both cases. Furthermore, the pancreaticobiliary tracts were entirely free. In case 1 a moderate, smooth atrophy of the liver was present; on section, one cherry-sized fibrous nodule was found in the right lobe. Histologically the liver disclosed two impressive lesions, the characteristics of which can be briefly outlined. Both lesions were restricted practically to the parenchyma. They were primarily degenerative. In the first lesion all the lobules were commonly involved. Within the individual lobule the most prominent changes were located in the central zone. Except for scattered areas of regressive changes, the remainder of the lobule was fairly well preserved. In contrast to the diffuse and zonal distribution of the first lesion, the second lesion was strictly focal. Within its confines, though, entire lobules had been destroyed; only their collapsed and fibrosed framework along with proliferating bile ducts persisted. While on first glance the two lesions differed widely in extent and structure, finer analysis showed that each, with its development retraced, represented a different stage in the same pathogenic process. First, degeneration and necrosis of parenchymal cells had taken place. In the diffuse lesion the central zones were chiefly involved; in the focal lesion whole lobules had been affected. Cellular and nuclear débris was removed by autolysis and reactive inflammation; collapse of stroma, fibrosis and attempts at regeneration followed. Jaundice was the sequel of hepatocellular dystrophy and architectural disorganization of biliary canaliculi. The age of the diffuse lesion could be reasonably placed at several weeks; the focal lesion seemed to have required a longer time to develop. In other words, the diffuse lesion satisfactorily accounted for the jaundice which had first appeared seven weeks before the patient's death and had persisted for three weeks, to result in clinical recovery.

Whether the focal lesion was related to the remote jaundice remained a matter for conjecture.

In case 2 macroscopic examination showed that both the liver and the spleen were enlarged. Microscopically the liver showed a progressive dystrophy. Histologically and pathogenetically the hepatic changes were altogether similar to those in case 1 except that they were more active and more diffuse within each lobule. In case 1 acute regressive and reactive inflammatory changes were minimal; the reticulum was collapsed. In case 2 active degeneration, necrosis and extensive secondary inflammation were the principal processes. The sinusoids were not collapsed, but dilated. In addition a distinct inflammatory and proliferative reaction was still noted in the portobiliary tissue. These histologic differences could be explained by the fact that the specimen from the liver of the first patient was obtained four weeks after recovery from mild jaundice of short duration, while in case 2 biopsy was made at the height of a marked icterus that was yet to run a prolonged course.

With the failure to demonstrate spirochetes and bacteria in our sections, the action of a toxin was necessarily postulated to explain the degenerative hepatic lesions. Besides bismuth, arsphenamine was the only significant drug taken by each patient. Arsenic was found in the urine. The histologic lesions in both cases resembled closely those observed in fatal cases of jaundice immediately following injection of arsphenamine and those obtained with the same drug in experiments with animals. On the other hand, our descriptions of the histologic pictures coincide also with the observations recently reported in cases of catarrhal jaundice of obscure toxic etiology.

CLINICOPATHOLOGIC CONCLUSIONS

Diagnosis.—Consideration of our cases does not validate the practice of various observers to include all cases of nonfatal jaundice which develop some time after arsphenamine therapy in one etiologic and anatomic group. Rather, each patient, especially because of the prognostic and therapeutic questions involved, should be looked on as presenting an individual diagnostic problem. In some instances the etiology of the icterus appears obvious. In others clinical appraisal must be limited to the exclusion of certain causes. Perhaps in cases in which separate factors of varying influence seem to play parts clinical appraisal can attempt to measure the respective importance of each. Even with a pathologic study, the quest for a specific cause may prove elusive. For example, in our two cases, hepatic syphilis, syphilitic hepatorecurrence, Herxheimer reaction, cholelithiasis, cholangeitis and tumor were ruled out. Gross and histologic examination proved that the

anatomic basis for the jaundice was intrahepatic parenchymal degeneration and necrosis due to some toxic agent. Designation of the particular toxin in each case, however, could not transcend a surmise drawn from a correlation of the known clinical, pathologic and experimental data. In case 1 arsphenamine appeared to be the culpable factor, yet so-called catarrhal jaundice also had to be thought of. In case 2 catarrhal jaundice seemed to be the most likely cause. But could a delayed effect of arsphenamine be entirely disregarded?

In respect to the modern conception of catarrhal jaundice as an intrahepatic regressive process our two cases assume a somewhat corroborative rôle.

The appearance of severe pain with acholic stools in case 2 illustrates the fact that rarely so-called toxic hepatitis presents a picture simulating that of cholelithiasis. Such a picture ought to be evaluated with care and perspective. A misdirected laparotomy may not always be harmless to the patient.

Prognosis.—In recent years confidence has often been placed in various tests for hepatic function for estimating the degree of damage to the liver and the time for resumption of treatment. Attention must be called to the discrepancy between the results of certain tests for hepatic function and the actual presence of hepatic damage in our case 1. In both cases a question arises as to permanent injury to the liver, subsequent recurrences of jaundice and toxic cirrhosis in nonfatal jaundice associated with arsphenamine therapy.

Therapy.—For patients with damage to the liver, as here reported, arsphenamine therapy is contraindicated.

LEUKONYCHIA TOTALIS

REPORT OF A CASE

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Leukonychia totalis is a rare condition of the nails. Eller and Anderson [1] in a review of the literature were able to find approximately fifty cases reported, seven of which occurred in the United States. Maukai [2] stated that only two cases of leukonychia totalis have been reported in Japan. The essential pathologic finding, as the name implies, is an entirely white nail. The color of the nails is described by various authors as being bluish white, chalky, ebony, ivory and milk-white.

This condition of the nails is usually found in young persons and is either congenital or acquired. The exact etiologic factor is not known, but generally the disorder has occurred in association with conditions such as typhoid, anemia, chronic arthritis with rheumatic endocarditis, measles, multiple neuritis, febrile diseases associated with malnutrition, trophic disorders and trauma. In the cases reported there has often been present a dermatologic condition, such as vitiligo or alopecia.

The earlier writers believed that the pathologic change was due to an absorption or imbibition of air into and between the nail cells; but Unna,[3] cited by Heller,[8] stated the belief that this absorption of air was only a secondary phenomenon, the primary cause of the lesion being a softening of the nail substance. Heidingsfeld,[4] on the other hand, was of the opinion that the condition was due to an improper keratinization of the nail cells without absorption of air. Becker [5] showed by microscopic examination the absence of air spaces and the presence of large-nucleated cells which took only acid stains. Singer [6] offered as an

1. Eller, J. J., and Anderson, N. P.: Leuconychia Totalis: Clinical Report with a Review of the Literature, M. J. & Rec. **127**:318 (March 21) 1928.

2. Maukai, T.: Leuconychia, Acta dermat. **16**:389, 1930.

3. Unna: Cited by Heller.[8]

4. Heidingsfeld, M. L.: Leucopathia Unguium, J. Cutan. Dis. **18**:490, 1900.

5. Becker, S. W.: Leukonychia Striata: Report of a Congenital Case, Arch. Dermat. & Syph. **21**:957 (June) 1930.

6. Singer, P. L.: Leukonychia: Its Normal Occurrences and Causation, Arch. Dermat. & Syph. **24**:112 (July) 1931.

explanation for the earlier idea of the absorption of air the belief that the strong nitric acid used in the technic for softening the nail dissolved the keratohyalin, thus leaving an air space between the layers of insoluble keratin. Singer [6] further stated in his summary: "As keratinization is due to decreased metabolism of the germinal layer, any increase in the metabolic rate will delay this, keratohyaline granules will persist, and leukonychia will result."

Fig. 1.—The toe-nails were bluish white, but on the second toe and the little toe of the left foot the nail had a pinkish cast. No lunula could be distinguished.

Fig. 2.—The finger-nails were bluish white. The nail of the right index finger had a pinkish cast. No lunula could be distinguished. At the time the nails were photographed there was an abrasion of the cuticle of the right index finger, which can be seen in the illustration.

Josephson and Lerner [7] were impressed with the frequency of leukonychia in association with diseases of the upper respiratory tract. They concluded that leukonychia probably has some relation to a metabolic disorder, as seen in its appearance with chronic colds when the acid-alkali balance was upset in the direction of alkalosis.

7. Josephson, E. M., and Lerner, C.: Leukonychia and "Colds": Secondary to Disturbances of Metabolism, Arch. Dermat. & Syph. **29**:703 (May) 1934.

No definite or specific therapeutic treatment is known. Heller [8] reported the use of a dusting powder, stannous oxide (10 parts) and carmine (0.1 part), as suggested by Joseph, and also an alcoholic solution of eosin. Colored nail polishes have also been used.

REPORT OF CASE

History.—M. L., a girl aged 14, was seen in January 1935 and gave the history of having entirely white finger-nails from the age of 4 years. During recent years her toe-nails had turned white. Her mother stated that prior to the age of 4 years, the nails, were apparently normal, and she believed that the condition followed exposure to severe cold. No member of the family was known to have any abnormality of the nails. The patient complained of no subjective symptoms.

Both parents were alive and well. The mother had an enlarged simple goiter.

The patient had measles and chickenpox at the age of 3 years, whooping cough at 6, scarlet fever at 7 and acute sinusitis at 8. Appendectomy was performed when she was 10 (1931).

Physical Examination.—The patient was a well developed and well nourished girl, weighing 102 pounds (46.3 Kg.). The general physical examination revealed no abnormality.

Nails: All of the nails of the fingers and toes were bluish white. The nails of the right index finger and the second toe and the little toe of the left foot had a pinkish cast. No lunula could be distinguished. At the time the nails were photographed there was an abrasion of the cuticle of the right index finger, which can be seen in the illustration. The nails were not brittle, and there was no fraying of the edges. The surface was smooth and somewhat flattened. No grooves or irregularities could be observed. The thickness of the nails seemed to be average.

SUMMARY

A review of the literature is given.

A case of leukonychia totalis is reported.

Dr. Hans Schwartz and Dr. Henry Niles confirmed the diagnosis.

8. Heller, J.: Die Krankheiten der Nägel, Berlin, A. Hirschwald, 1900, p. 89.

A RAPID METHOD OF STAINING SPIROCHAETA PALLIDA IN SINGLE SECTIONS OF TISSUE

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LOS ANGELES

In 1933, I described a method,[1] a modification of Dieterle's [2] technic, for demonstrating Spirochaeta pallida in single microscopic sections, in which the use of uranium nitrate as a preliminary mordant, originally described by Jahnel,[3] prevents the impregnation of nerve fibers in sections of the central nervous system so that they do not obscure the spirochetes in the subsequent impregnation with the silver salts.

More recently several features of the technic have been improved, adding materially to the certainty of result without increasing the time involved. The entire procedure, including the fixation of fresh tissue, can be completed in one and one-half hours.

IMPROVED TECHNIC

Drop fresh blocks of tissue about 5 mm. thick in a 10 per cent solution of formaldehyde heated to 67 C. (152.6 F.) and fix in an oven at 67 C. for ten minutes. (Tissues already fixed with formaldehyde do not require this treatment.)

Cut thin sections, from 5 to 10 microns, on a freezing microtome and place them in a 1 per cent aqueous solution of sodium cobalti-nitrite for five minutes.

Wash the sections in two changes of distilled water.

Place them in the following (no. 1) solution for fifteen minutes at 67 C.:

Uranium nitrate	1 Gm.
Formic acid (chemically pure), 85 per cent	3 cc.
Glycerin (chemically pure)	5 cc.
Acetone	10 cc.
Alcohol, 95 per cent	10 cc.

Wash in two changes of distilled water.

Place the sections in a 0.75 per cent aqueous solution of silver nitrate for one hour at 67 C.

Rinse rapidly in distilled water.

Place the sections for three minutes in 2 cc. of the developing solution, to which prior to use add 1 drop of egg albumin-glycerin fixative and thoroughly mix. (The egg-albumin-glycerin fixative is that commonly used in fixing paraffin sec-

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From the Los Angeles County General Hospital.

1. Krajian, A. A.: A Modification of Dieterle's Method for Demonstrating Spirochaeta Pallida in Single Microscopic Sections, Am. J. Syph. & Neurol. **17**: 127, 1933.

2. Dieterle, R. R.: A Method for Demonstration of Spirochaeta Pallida in Single Microscopic Sections, Arch. Neurol. & Psychiat. **18**:73 (July) 1927.

3. Jahnel, F.: Studien über progressive Paralyse, Arch. f. Psychiat. **57**:847, 1917.

tions to slides.) While developing, work under a 60 watt electric lamp 4 feet above the specimen and expose the developing solution to light about fifteen minutes before it is to be used. The composition of the developing solution is as follows:

Hydroquinone	0.31 Gm.
Sodium sulphite	0.06 Gm.
Acetone	2.5 cc.
Solution of formaldehyde (chemically pure) 40 per cent, made neutral	2.5 cc.
Pyridine	2.5 cc.
Saturated solution of mastic in 95 per cent alcohol	2.5 cc.
Distilled water	15.0 cc.

Wash for a few seconds in distilled water.

Place the sections in the 0.75 per cent solution of silver nitrate previously used from 15 to 25 seconds.

Wash in two changes of distilled water.

Draw the sections onto slides and blot with fine filter paper; dehydrate in absolute alcohol for two minutes and then blot and clear in pure xylene for two minutes.

Mount the section in dammar resin.

COMMENT

The sections should be cut quite thin, preferably from 5 to 10 microns in thickness, as thicker sections make demonstration of spirochetes difficult owing to the fat content.

The purpose of using acetone and alcohol in the no. 1 solution is to remove any fatty substance present in the tissue, especially in sections of liver and brain.

The temperature of the oven is important; 67 C. has proved to be optimum. Lower temperatures require a longer time, while 70 C. or above has resulted in failure to demonstrate spirochetes in known control tissue.

Both the no. 1 solution and the solution of silver nitrate should be warmed to 67 C. before sections are placed in them. The no. 1 solution requires fifteen minutes and the solution of silver nitrate about thirty minutes to be heated to 67 C. Therefore, in order to save time it will be a good practice to place the solutions in the oven before one begins to cut sections.

Control sections should always be prepared from material known to contain spirochetes.

The developing solution when made up fresh is a creamy color but soon it turns brown. The solution keeps well from two to three weeks in a dark cool place. After that it begins to deteriorate, the mastic separating and settling to the bottom of the container. When this occurs, a fresh supply should be prepared.

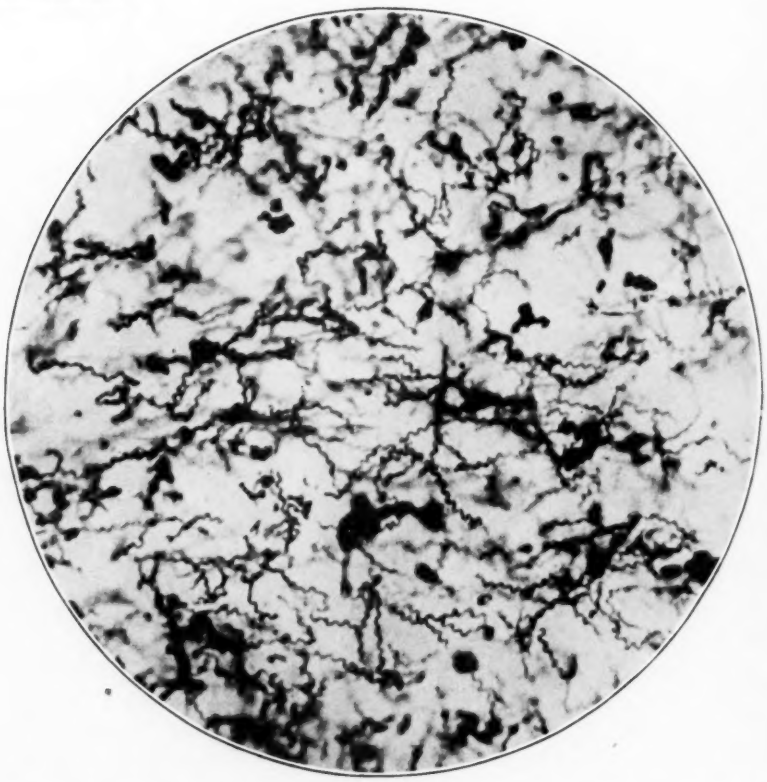
The no. 1 solution is stable and keeps indefinitely.

Sodium cobalti-nitrite solution is not stable and should be made fresh each time.

All solutions and reagents should be kept in a dark cool place, preferably in a cabinet with black walls.

EXAMINATIONS OF SECTIONS

In primary lesions, it is comparatively easy to find spirochetes in large numbers, and generally one or two sections will be sufficient for examination.



Photomicrograph showing Spirochaeta pallida from a specimen of the liver of a patient with congenital syphilis, stained by the method described.

With chronic lesions, half a dozen or more sections should be prepared and carefully searched.

In the examination of certain lesions suspected of being syphilitic, my attention has been called to another possible use of this silver stain, which has not to my knowledge been heretofore emphasized. It was noted that various bacteria and related forms, including gram-negative and gram-positive organisms, are made readily visible. Those observed

have included a streptothrix in a cutaneous lesion, a gonococcus in endocardial vegetations and Bacillus influenzae in acute meningitis. All of these were gram-negative organisms not readily demonstrated by a Gram-Weigert stain.

RESULTS

The chief advantages of this method are the ease and rapidity with which it can be done and the greater degree of certainty of the results. It is far superior to the Levaditi method.

After more than three years of constant use, the method has proved satisfactory for the demonstration of Spirochaeta pallida in biopsy as well as in autopsy material. A large series of primary syphilitic lesions have been examined histologically, as well as numerous secondary and tertiary syphilitic lesions.

CLINICAL SPECTROSCOPY

QUANTITATIVE DISTRIBUTION OF GOLD IN THE BODY OR ITS PHYSIOPATHOLOGIC RETENTION AS A RECIPROCAL OF THE CAPILLARY SYSTEM

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In a recent publication [1] evidence was submitted which proved that regardless of the site—arm, leg, abdomen, flank, chest or back—from which a specimen of skin for biopsy was obtained, the quantity of gold in the specimen was directly proportional to the total dosage administered. Likewise, when several specimens for biopsy from the leg and lumbar region and from the forearm and lumbar region were obtained from the same patient, the respective specimens showed an equal quantity of gold, proving the uniform distribution in the cutis. Further, it was found that gold remained permanently fixed in the cutis or connective tissue, the factor of time after the last injection being irrelevant. Recently there have been reports in the literature describing a peculiar violaceous tint of the exposed skin in patients living in Alpine regions who had received treatment with gold compounds. If a solution of gold sodium thiosulphate is exposed to artificial ultraviolet radiation an identical color will result. A similar phenomenon is seen in the development of argyrosis. Gold can be detected in a biopsy specimen after the patient has received a total dosage equivalent to somewhere between 0.05 and 0.1 Gm. of gold sodium thiosulphate. When there is a history of therapy with a gold compound but the total dosage is unknown, the quantity which had been administered previously can be determined by a biospectrometric analysis.[2] Since gold is not present normally in connective tissue, its presence always indicates previous therapy.

From the Division of Dermatology and Syphilology, Skin and Cancer Unit, New York Post-Graduate Medical School and Hospital, Columbia University, Dr. George Miller MacKee, director.

1. Gaul, L. E., and Staud, A. H.: Clinical Spectroscopy: A Study of Biopsy Material Taken from Patients Receiving Gold Sodium Thiosulphate, Arch. Dermat. & Syph. **28**:790 (Dec.) 1933.

2. The word biospectrometric specifies a quantitative spectrographic analysis for the metallic constituents in differentiated and undifferentiated mesoderm, obtained by taking a dermal biopsy specimen weighing approximately 0.025 Gm. with a 3/16 inch (0.47 cm.) punch.

Three basic facts will now be presented: (1) the purport of metallic retention or the physiopathologic disposition of a metal (gold); (2) the mode of excretion, and (3) the distribution of the metal in the body as a reciprocal of the capillary system.

Metallic retention is the physiopathologic disposition of a metallic element around the capillaries. These endothelial tubes or capillaries originate, as do all connective tissue structures, from embryonic mesenchyme. They penetrate everywhere between the elements of various organs and tissues and are accompanied along their entire course by connective tissue cells and layers of thin collagenous or reticular fibers which form a thin membranous sheath around the capillaries and separate them from the elements of other tissues.[3] While this interpretation portrays the utter vastness of the area for metallic retention, the actual elements concerned in this process are the connective tissue cells. These cells belong to the so-called reticulo-endothelial system and are peculiar in that they retain their embryonic characteristics throughout adult life. They have been called adventitial cells,[4] pyrrhol cells,[5] clasmatocytes,[6] rhagiocrine cells,[7] resting wandering cells,[8] macrophages[9] and histiocytes.[10] Recent investigations and contributions concerning the rôle of the reticulo-endothelial system in health and disease, especially in the infectious processes, have attributed such similar and vital functions to this system that only the part played by these cells in the storage and distribution of colloidal metals will be considered briefly.

On the introduction of vital staining, Ribbert[11] showed that the histiocytes have specific powers to store and distribute lithium carmine. Goldmann[5] observed a similar phenomenon, using pyrrhol blue. The histiocytes were further interpreted by Aschoff and Kiyono[12] in a report

3. Maximow and Bloom: A Textbook of Histology, ed. 2, Philadelphia, W. B. Saunders Company, 1934.

4. Marchand, F.: Ueber Clasmatocyten, Mastzellen und Phagocyten des Netzes, Verhandl. d. deutsch. path. Gesellsch. **4**:124, 1901.

5. Goldmann, E. E.: Die äussere und innere Sekretion des gesunden und kranken Organismus im Lichte der vitalen Farbung, Beitr. z. klin. Chir. **64**:192, 1909.

6. Ranvier, L.: Des clasmatocytes, Arch. d'anat. micr. **3**:122, 1900.

7. Renaut, J.: Les cellules connectives rhagiocrines, Arch. d'anat. micr. **9**:495, 1907.

8. Maximow, A.: Ueber die Zellformen des lockeren Bindegewebes, Arch. f. mikr. Anat. **67**:680, 1906.

9. Evans, H.: The Macrophages of Mammals, Am. J. Physiol. **37**:243, 1915.

10. Kiyono, K.: Zur Frage der histiozytaren Blutzellen, Folia haemat. **18**: 149, 1914.

11. Ribbert, H.: Die Abscheidung intravenös injizierten gelosten Karmins in den Geweben, Ztschr. f. allg. Physiol. **4**:201, 1904.

12. Aschoff, and Kiyono, K.: Die vitale Karminspeicherung, Jena, Gustav Fischer, 1914.

on the vital staining characteristics of these cells in normal and pathologic tissues. Maximow [13] described the intimate relation between the blood, the connective tissue and the wandering characteristics of the histiocytes, and he interpreted the storing of vital dyes as a special case of their "defense" activity. Cappell [14] observed the capacity of the histiocytes for ingesting and storing such substances as trypan blue, isamine blue, vital new red, india ink, carmine particles and the oxides of iron. Bouffard [15] was able to demonstrate their staining characteristics with the benzidine dyes. Slavjansky [16] identified the histiocytes by using cinnabar, red mercuric sulphide. Tschaschin,[17] in 1914, presented a review of the literature which showed that if certain substances, such as colloidal metals and various dyes, are injected into the blood they are deposited chiefly in connective tissue and electively in certain cellular elements of the tissues, or histiocytes. He reported his own experiments with vital staining, using collargol and trypan blue with rabbits and isamine blue with white rats (figure). Other observers have reported similar findings with thorium dioxide,[18] colloidal copper,[19] silver,[20] gold,[21] iron,[22] bismuth [23] and mercury.[24]

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13. Maximow, A. A.: Relation of Blood Cells to Connective Tissue and Endothelium, Physiol. Rev. **4**:533, 1924.

14. Cappell, D. F.: Reticulo-Endothelial System in Light of Vital Staining, Glasgow M. J. **114**:209, 1930.

15. Bouffard, G.: Injection of Benzidine Dyes in Normal Animals, Ann. Inst. Pasteur **20**:539, 1906.

16. Slavjansky, K.: Experimentelle Beiträge zur Pneumonokoniosislehre, Virchows Arch. f. path. Anat. **48**:326, 1869.

17. Tschaschin, S.: Über die ruhenden Wanderzellen und ihre Beziehungen zu den anderen Zellformen des Bindegewebes und zu den Lymphozyten, Folia haemat. **7**:317, 1913-1914.

18. Wen, I. C., and Jung, T. S.: Reactions of Blood and Tissue Cells to Colloidal Thorium Dioxide, Chinese J. Physiol. **8**:85, 1934. Hanke, H.: Experimentelle Untersuchungen biologischer Abwehrvorganze bei Thoriumdioxydspeicherung des Reticuloendothels, Ztschr. f. d. ges. exper. Med. **88**:391, 1933.

19. Kritschewski, I. L.; Zscherikower, R. S., and Dwolaizkaja-Barischewa, K. M.: Ueber eine noch unbekannte Funktion des retikulo-endothelial Systems, Ztschr. f. Immunitätsforsch. u. exper. Therap. **81**:163, 1933. Lo Cascio, G.: Rapporto tra azione sul tessuto emopoietico e fissazione nell'apparato reticoloendoteliale del solfuro di rame colloidale, Boll. d. Soc. ital. di biol. sper. **5**:819, 1930. Letterer, E.: Ueber die Wirkung von elektrolloidalem Kupfer auf das reticulo-endotheliale System, Klin. Wchnschr. **12**:597, 1933.

20. Tschaschin.[17] Orestano, G.: Ricerche quantitative sull-attività granulopessica dell'apparato r.e. epatico del Dott, Boll. d. Soc. ital. di biol. sper. **5**:818, 1930. Bagnaresi, G.: Reticolo-endotelio e ricambio lipoides e gassoso, Folia med. **16**:981, 1930. Stewart, F. W., and Parker, F.: So-Called "Endothelial Blockade" with Collargol: An Immunologic and Histologic Study, Am. J. Path. **2**:381, 1926.

21. Schamberg, J. F.: Chrysoderma, Arch. Dermat. & Syph. **18**:862 (Dec.) 1928.

At this point it is well to mention certain modifying factors influencing the localization and distribution of metals. Probably the most important factor is the degree or extent of response or proliferation of connective tissue. This can be illustrated by several examples of patients who during a course of silver therapy happen to receive an injury of the exposed areas which heals by second intention but which produces a discoloration at the site first. Biospectrometrically this area shows

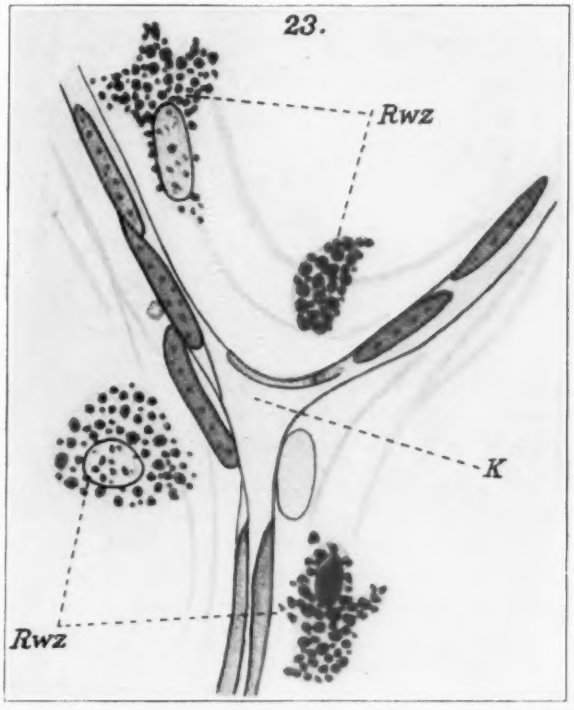

Diagram showing the mesentery of a rat after injections of collargol (colloidal silver), illustrating the cellular elements concerned in effecting the storage and distribution of colloidal metals. *K* means capillary, and *Rwz*, histiocytes. (After Tschaschin[17]).

22. Cappell.[14] Radt, P.: Ueber die körnige Ablagerung kolloider Farbstoffe in den Leberparenchymzellen von Kaninchen nach intravitaler Injektion (nach Versuchen mit Tusche und Eisen), Ztschr. f. d. ges. exper. Med. **69**:721, 1930. Weiss, S., and Sumegi, S.: Untersuchungen über die Funktion des mit Eisen blockierten reticuloendothelialen Apparates, Wien. Arch. f. inn. Med. **10**:457, 1925.

23. Califano, L.: Untersuchungen über die Speicherung im retikulo-endothelialen System mit kolloidalem Wismut, Krankheitsforschung **6**:77 (April) 1928.

24. Slavjansky.[16] Goldzieher, M. A., and Peck, S. M.: Experimental Studies on the Reticulo-Endothelial System: Effect of Mercury Salts and Sulpharsphenamine on the Reticulo-Endothelial Cells, Arch. Path. **3**:635, 1927.

a greater amount of silver. Children absorbing lead [25] or receiving therapy with bismuth [26] will show roentgenographic evidence of these metals at the ends of growing bones. Another factor to be considered is the metabolic and functional activity of various organs and tissues, which necessitates a greater density of the capillary network with a concomitant flow of a greater volume of blood, thereby providing an increased area for the distribution of a metal as well as favoring its localization.

While the physiopathologically retained metals, such as gold, are distributed electively by the histiocytes about the capillary system, elimination of them from the body also becomes a cellular response provided they are present as colloidal particles. The ubiquitous histiocytes, assisted by the more highly differentiated cellular elements arising from the primitive reticular cells in lymphoid and myeloid structures as well as the circulating leukocytes of the blood, aid in freeing the system from noxious agents, bacteria, foreign proteins, particulate matter and colloidal metals.[27] The avenue of escape is by diapedesis through the linings of the mucous membrane of the lungs,[28] the mouth, the gastrointestinal tract [29] and the genito-urinary tract.[30] When it is considered

25. (*a*) Vogt, E. C.: A Roentgen Sign of Plumbism, Am. J. Roentgenol. **24**:550, 1930. (*b*) Vogt, E. C.: Roentgenologic Diagnosis of Lead Poisoning in Infants and Children, J. A. M. A. **98**:125 (Jan. 9) 1932. (*c*) Park, E. A.; Deborah, J., and Kajdi, L.: Shadows Produced by Lead in X-Ray Picture of the Growing Skeleton, Am. J. Dis. Child. **41**:485 (March) 1931. (*d*) Park, E. A.; Jackson, D.; Goodwin, T. C., and Kajdi, L.: X-Ray Shadows in Growing Bones Produced by Lead, J. Pediat. **3**:265, 1933. (*e*) Caffey, J.: Clinical and Experimental Lead Poisoning, Radiology **17**:957, 1931. (*f*) Childe, A. E.: The Roentgen Ray Diagnosis of Lead Poisoning in Children, Internat. Clin. **1**:192, 1934.

26. Vogt.[25a] Tisdall, quoted by Park and others.[25d]

27. Maximow, A. A.: Morphology of Mesenchyme Reaction, Arch. Path. **4**:557, 1927. Foot, N. C.: The Endothelial Phagocyte, Anat. Rec. **30**:15, 1925.

28. Slavjansky.[16] Tchistovitch, N.: Des phénomènes de phagocytose dans les poumons, Ann. Inst. Pasteur **3**:337, 1889. Permar, H. H.: An Experimental Study of the Mononuclear Phagocyte of the Lungs, J. M. Research **42**:9, 1920-1921; The Development of the Mononuclear Phagocyte of the Lung, ibid. **42**:147, 1920-1921; The Migration and Fate of the Mononuclear Phagocyte of the Lungs, ibid. **42**:209, 1920-1921; The Function of the Endothelial Cells in Pathological Conditions, Especially Tuberculosis, Am. Rev. Tuberc. **9**:507, 1924. Haythorn, S. R.: Some Histological Evidences of the Disease Importance of Pulmonary Anthracosis, J. M. Research **29**:257, 1913-1914.

29. Blumberg, H., and Carey, T. N.: Argyremia, Detection of Unsuspected and Obscure Argyria by the Spectrographic Demonstrations of High Blood Silver, J. A. M. A. **103**:1521 (Nov. 17) 1934. Isaacs, R., and Danielian, A.: Maintenance of the Leukocyte Level and Changes During Irradiation: Study of the White Blood Cells Appearing in Saliva and Relative to Those Appearing in the Blood, Am. J. M. Sc. **174**:70, 1927. Dukes, C., and Bussey, H.: The Number of Lymphoid Follicles of the Human Large Intestine, J. Path. & Bact.

that the circulating lymphocytes remain constant and that more lymphocytes enter the blood from the thoracic duct in twenty-four hours than are present in the blood at any one time, exclusive of the leukocytes from other lymphoid and myeloid structures, it becomes quite obvious that all of these cells cannot be destroyed by the system but that they are eliminated by diapedesis with their phagocytosed waste products, colloidal metals and other noxious agents.[31]

These observations and many others have contributed evidential data sufficient to prove that the cellular elements are concerned in effecting the distribution, localization and excretion of colloidal metals. This physiologic response of the cellular elements to a colloidal metal is the same, irrespective of the source of entry to the lymphatic or blood stream, i. e. absorption from the alveoli of the lungs or from the gastrointestinal tract and intravenous or intramuscular administration.

A composite picture which will serve as an excellent illustration of the distribution of a colloidal metal as a reciprocal of the capillary system is furnished by histologic studies in cases of argyria. The chemical and physical properties of silver are such that when this metal is absorbed or given intravenously a beautiful elective staining of the tissues occurs. The metal is seen lying free in the connective tissue spaces and in the histiocytic cells. The agglomeration at certain points is most likely due to a cytolysis of the cells freeing the particles of silver, which are again phagocytosed with subsequent migration or left lying free in the tissues.

The principal objective which culminates the biospectrometric study of the distribution of gold in the body signalizes this fact. After a biopsy specimen had been shown to have a retention of silver equivalent to that given by 8 Gm. of silver arsphenamine,[32] subsequent histologic and spectrographic studies of the various tissues and organs confirmed the presence of silver and indicated the distribution as a reciprocal of the capillary system easily visible owing to its chemical and physical properties. In a second biopsy specimen in which a biospectrometric

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29:111, 1926. Nagao, K.: The Fate of India Ink Injected into the Blood, J. Infect. Dis. **27**:527, 1920; The Fate of India Ink Injected into the Blood: The Formation of Intracellular Granules and Their Movements, ibid. **28**:294, 1921.

30. Addis: The Number of Formed Elements in Urinary Sediment of Normal Individuals, J. Clin. Investigation **2**:409, 1926.

31. Bunting, C. H., and Huston, J.: The Fate of the Lymphocyte, J. Exper. Med. **33**:597, 1921.

32. Gaul, L. E., and Staud, A. H.: Clinical Spectroscopy: A Study of Biopsy Material from Patients Who Had Received Intravenous Injections of Silver Arsphenamine, Arch. Dermat. & Syph. **30**:433 (Sept.) 1934; Clinical Spectroscopy: Seventy Cases of Generalized Argyrosis Following Organic and Colloidal Silver Medication Including a Biospectrometric Analysis of Ten Cases, J. A. M. A. **104**:1387 (April 20) 1935.

analysis proved that there was a retention of gold approximately equal in amount to the retention of silver already mentioned, the gold was invisible histologically owing to its chemical and physical properties. Although the two samples contained equivalent amounts of metal around the capillaries and in the tissue spaces, only the silver could be seen readily during the histologic examination. When a suitable staining technic is developed for gold in histologic sections; its visualization will confirm the spectrographic findings shown in the accompanying table.

Biospectrometric Analysis of Autopsy Material *

Parts of Body Analyzed	Amount of Gold in a 0.025 Gm. Specimen, Gm.
Fascia	0.000000002
Sacral plexus	0.000000002
Skin (shoulder)	0.000000003
Muscle (longus colli)	0.000000002
Liver	0.000000005
Kidney	0.000000004
Medulla of a rib	0.000000002
Cervical portion of cord	0.000000001
Vertebral cortex	0.000000001
Cerebral cortex and meninges†	0.00000001

* The autopsy material was furnished by Dr. George Ornstein, Metropolitan Hospital, Welfare Island, Department of Tuberculosis, New York City. L. J., a colored man aged 35, was admitted to the hospital on March 4, 1933. His condition was diagnosed as pulmonary tuberculosis with bilateral cavitation. On March 11 the patient received 0.05 Gm. of gold sodium thiosulphate. A biospectrometric analysis a week later gave negative results for gold. On March 18 a second injection of 0.05 Gm. was administered. After a week had elapsed a second biospectrometric analysis gave positive results for gold, which established the sensitivity for gold spectrographically as occurring somewhere between 0.05 and 0.1 Gm. of gold sodium thiosulphate. A month later autopsy specimens were obtained. These were secured from fresh material with a 3/16 inch (0.47 cm.) dermal punch. Each specimen was immediately placed in a previously cleaned pyrex test tube, which was corked. Specimens of sputum, feces and urine were collected after each injection and subsequently ashed. A spectographic analysis showed approximately an equal excretion through the lungs and gastro-intestinal tract and only a trace excreted by the kidneys. Photometric determinations were not made.

† This material came from another group of autopsy specimens.

CONCLUSIONS

The quantitative distribution of gold in the body is directly proportional to the total dose administered.

Attention has been called to the factors modifying the distribution and localization of colloidal metals, such as gold.

The physiopathologic retention of gold as a reciprocal of the capillary system has been ascribed to the physiologic rôle of cellular elements, principally the histiocytes.

The excretion of gold likewise has beeen interpreted as a cellular response.

A biospectrometric analysis for establishing the comparative retention of gold and silver substantiates a similar distribution.

A spectrographic analysis of autopsy material proves a corollary to a biospectrometric analysis, since it establishes the fact that the quantity of gold in the biopsy specimen represents the quantitative distribution or retention in the body.

CLINICAL SPECTROSCOPY

QUANTITATIVE DISTRIBUTION OF SILVER IN THE BODY OR ITS PHYSIOPATHOLOGIC RETENTION AS A RECIPROCAL OF THE CAPILLARY SYSTEM

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AND

A. H. STAUD, B.S.

NEW YORK

Metallic retention has been defined as the physiopathologic disposition of metallic elements around the capillaries of the blood vascular system. The reciprocity between the capillary and the metallic distribution not only results in the metals being placed contiguous to the cellular elements of various vital organs and tissues but implies the vastness of the area for the retention of metallic constituents by the body. This interpretation disregards the mode of entry into the lymph or the blood stream but considers the dispensation of a metal as a function of its chemical and physical properties. When the biochemical state of a metal is colloidal, whether it is absorbed as an extraneous contamination or administered therapeutically, the retention has been ascribed to the physiologic rôle of cellular elements, principally the connective tissue cells or histiocytes. The excretion of colloidal metallic elements has also been interpreted as a cellular phenomenon.[1]

When it was established that the quantity of gold present in a specimen of the skin taken for biopsy was directly proportional to the total dosage administered,[2] a study under identical conditions proved a similar retention for silver.[3] It was also shown that, regardless of the cutaneous site—arm, thigh, chest or abdomen—from which the specimen was obtained, the quantity of silver in the sample was directly proportional to the total dosage of silver arsphenamine administered (fig. 1).

From the Skin and Cancer Unit, New York Post-Graduate Medical School and Hospital, Columbia University; George Miller MacKee, Director.

1. Gaul, L. E., and Staud, A. H.: Clinical Spectroscopy: The Quantitative Distribution of Gold in the Body or Its Physiopathologic Retention as a Reciprocal of the Capillary System, Arch. Dermat. & Syph., to be published.

2. Gaul, L. E., and Staud, A. H.: Clinical Spectroscopy: A Study of Biopsy Material Taken from Patients Receiving Gold Sodium Thiosulphate, Arch. Dermat. & Syph. **28**:790 (Dec.) 1933.

3. Gaul, L. E., and Staud, A. H.: Clinical Spectroscopy: A Study of Biopsy Material from Patients Who Had Received Intravenous Injections of Silver Arsphenamine, Arch. Dermat. & Syph. **30**:433 (Sept.) 1934.

Likewise, when several biopsy specimens were obtained from the same subject, the respective samples showed equal quantities of silver, proving the uniform distribution in the cutis. Further, it was observed that silver remained permanently fixed in the cutis or connective tissue. An

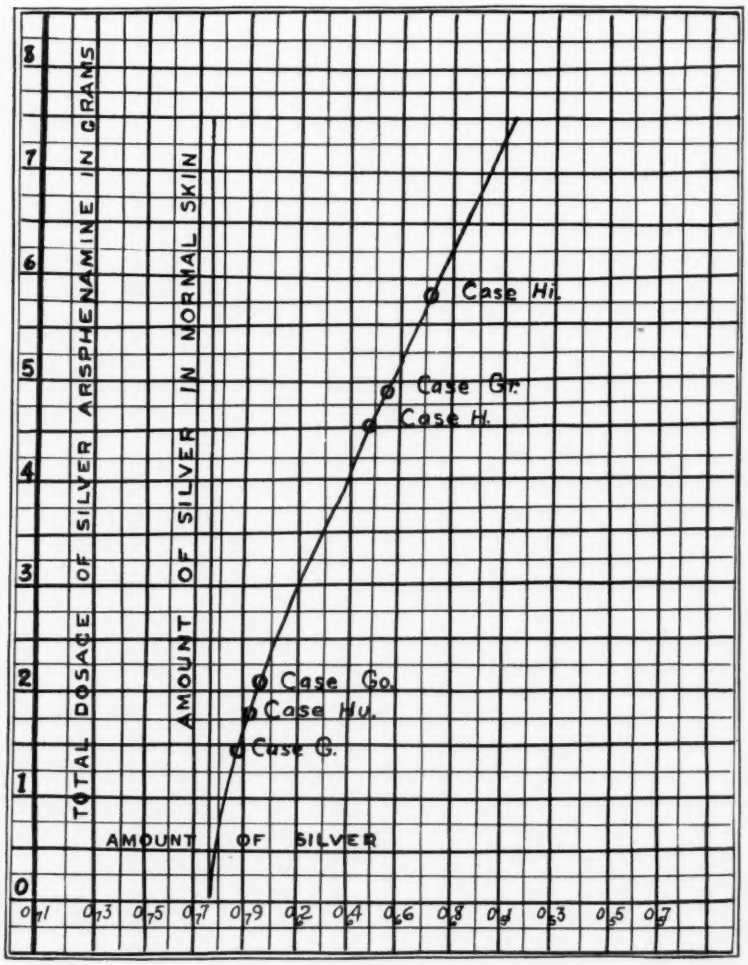

Fig. 1.—Graphic illustration of the quantitative retention of silver in specimens obtained for biopsy from patients receiving silver arsphenamine. The quantity of silver present in the biopsy specimens was directly proportional to the total dosage administered. The abscissas indicate the quantity of silver expressed in grams (from 0.00000001 to 0.000007 Gm.); the ordinates, the total dosage of silver arsphenamine administered and the quantity of silver present in specimens of apparently normal skin. In case *G*, the patient received 1.45 Gm.; in case *Go.*, 2.05 Gm.; in case *Gr.*, 4.9 Gm., and in case *Hi.*, 5.775 Gm., of silver arsphenamine.[2] Similar findings were reported for gold.[1]

interesting observation in this respect associates the degree of discoloration of the exposed parts in cases of argyria with the quantitative retention of silver, as determined in a biopsy specimen obtained from the region of the knee in which no discoloration was shown.[4]

The chemical and physical properties of silver are such that when this metal is absorbed or given intravenously beautiful and selective staining of the tissues occurs. Histologic studies of stained and unstained tissues and organs reveal the distribution of the silver as complementary or reciprocal to that of the capillary system.[5] The metal was seen lying free in the connective tissue spaces and in histiocytes. The agglomeration at certain points is probably due to cytolysis, by which the particles of silver are freed. They are again phagocytosed by cells which subsequently migrate, or they are left lying free in the tissues (fig. 2). At this point it is well to mention certain modifying factors influencing the localization and distribution of metals: the degree or extent of the response or proliferation of the connective tissue and the increased metabolic and functional activity of various organs and tissues, which necessitates a greater density of the capillary network with a greater concomitant volume of flow of blood. The presence of silver in the tissues has been identified by chemical and histochemical and recently by spectrographic methods.[6]

The distribution and localization of silver about the capillary system as seen in histologic studies in cases of argyria have been accepted as a classic and composite picture of what is meant by metallic retention.

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4. Gaul, L. E., and Staud, A. H.: Clinical Spectroscopy: Seventy Cases of Generalized Argyrosis Following Organic and Colloidal Silver Medication Including a Biospectrometric Analysis of Ten Cases, J. A. M. A. **104**:1387 (April 20) 1935.

5. Stewart, F. W., and Parker, F.: So-Called "Endothelial Blockade" with Collargol: An Immunologic and Histologic Study, Am. J. Path. **2**:381, 1926. Fromman, C.: Ein Fall von Argyria mit Silberabscheidungen in Darm, Leber, Nieren und Milz, Virchows Arch. f. path. Anat. **17**:135, 1859. Riemer, B.: Ein Fall von Argyria, Arch. d. Heilk. **17**:330, 1876. Kino, F.: Leberargyria universalis, Frankfurt. Ztschr. f. Path. **3**:398, 1909. Gettler, A. O.; Rhoads, C. P., and Weiss, Soma: A Contribution to the Pathology of Generalized Argyria with a Discussion of the Fate of Silver in the Human Body, Am. J. Path. **3**:631, 1927.

6. Sheldon, J. H., and Ramage, H.: Spectrographic Analysis of Human Tissue, Biochem. J. **25**:1608, 1931. Gerlach, Walther, and Gerlach, Werner: Der Elementnachweiss im Gewebe der Gold und Silbernachweiss im Gewebe, Virchows Arch. f. path. Anat. **282**:209, 1931. Zbinden, C.: Recherches spectrographiques sur des cendres de sangs et d'organes humains, Mém. Soc. vaudoise d. sc. nat. **3**:233, 1930. Blumberg, H., and Carey, T. N.: Argyremia, Detection of Unsuspected and Obscure Argyria by the Spectrographic Demonstration of High Blood Silver, J. A. M. A. **103**:1521 (Nov. 17) 1934.

Thus far, a significant fact has been established by biospectrometric[7] analysis. When the density of other metallic lines in the biospectrograms,[8] such as those of gold,[2] lead,[9] nickel,[10] copper, aluminum, zinc and tin,[11] is proportionate to that of the line for silver, which is histologically visible owing to its chemical and physical properties, provided its retention is sufficiently high, a similar quantitative retention of the aforementioned metals in the body is proved, but owing to their chemical

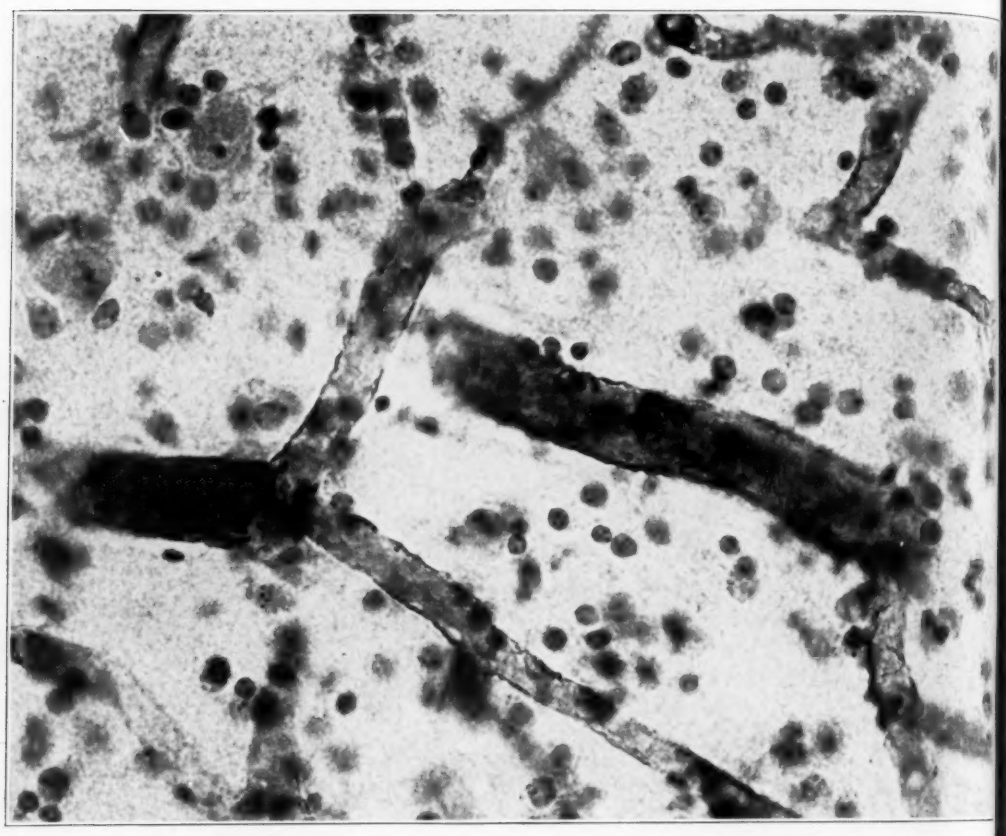

Fig. 2.—Photomicrograph of a section of the cerebral cortex, illustrating the distribution and agglomeration of particles of silver as a reciprocal of the capillary system. Silver was identified as such by chemical, histochemical and spectrographic methods. Courtesy Dr. Armin St. George.

7. The word "biospectrometric" specifies a quantitative spectrographic analysis of the metallic constituents in differentiated and undifferentiated mesoderm obtained by taking a biopsy specimen of skin with a 3/16 inch (0.47 cm.) dermal punch weighing approximately 0.025 Gm.

8. Gaul, L. E., and Staud, A. H.: Clinical Spectroscopy: The Advantages and Physical Principles of the Spectrograph with the Technic for Taking Specimen for Biospectrometric Analysis, Arch. Dermat. & Syph. **32**:385 (Sept.) 1935.

and physical properties they are histologically invisible, regardless of the quantity present. When suitable technics are developed for staining them, a distribution and localization will be shown histologically similar to those established biospectrometrically.

Quantitative Distribution of Silver in the Body *

Samples Analyzed	Quantity of Silver, Gm.
Skin of abdomen	0.00000001
Bone	
Rib, left ninth	
Cortex	0.00000001
Medulla	0.00000002
Temporal	0.00000001
Vertebra, twelfth dorsal	
Cortex	0.00000001
Medulla	0.00000002
Liver	0.00000001
Kidney, left	
Cortex	0.00000002
Medulla	0.00000002
Bladder	0.00000004
Spleen	
Cortex	0.00000005
Medulla	0.00000005
Muscle	
Abdominal	0.00000001
Heart, left ventricle	0.00000001
Longus coli	0.00000001
Ovary	0.00000001
Adrenal, left	0.00000001
Esophagus	0.00000001
Stomach	0.00000001
Small intestine	0.00000001
Large intestine	0.00000001
Gallbladder	0.00000001
Ear, left	0.00000002
Labyrinth	0.00000001
Ossicles	0.00000001
Frontal sinus	
Membrane	0.00000001
Brain	
Cerebral cortex, left hemisphere	0.00000001
Cervical portion of the cord	0.00000001
Optic nerve	0.00000001
Cartilage, trachea	0.00000001
Lung, left	
Apex	0.00000002
Base	0.00000002
Lymph node, cervical	0.00000002
Sacral nerve	0.00000001
Fascia of thigh	0.00000001

* Autopsy material was obtained from the fresh tissue with a 0.47 cm. carbon steel punch and was analyzed under identical physical conditions. An analysis of three other complete series of autopsy samples gave the following values for the quantitative retention of silver: 0.000000001, 0.00000006 and 0.00000001 Gm.

The purport of the spectrographic data shown in the table is to establish a corollary to the biospectrometric analysis; i. e., in determining the quantity of silver present in a biopsy specimen one determines the

9. Gaul, L. E., and Staud, A. H.: Clinical Sepectroscopy: A Spectrometric Analysis of Biopsy Specimens Obtained from Cases of Plumbism and Workmen in Daily Contact with Lead Paint, J. Nerv. & Ment. Dis. **81**:265, 1935.

10. Gaul, L. E., and Staud, A. H.: Clinical Spectroscopy: The Quantitative Retention of Nickel in Psoriasis, Arch. Dermat. & Syph. **30**:697 (Nov.) 1934.

11. Gaul, L. E., and Staud, A. H.: Unpublished material.

quantitative retention of that element throughout the various organs and tissues of the body.

SUMMARY AND CONCLUSIONS

Metallic retention has been defined as the physiopathologic disposition of metallic elements around the capillaries of the blood vascular system.

The distribution of silver as seen histologically has been accepted as a classic illustration of what is meant by metallic retention.

The quantitative distribution of silver in the body is directly proportional to the total dosage administered.

A corollary to a biospectrometric analysis has been established, since in determining the quantity of silver in a biopsy specimen one determines the quantitative retention of that element throughout the various tissues and organs of the body.

SKIN DISEASES AND THE WEATHER

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The pioneer work of Kraus, Zondek [1] and Petersen [2] stimulated me to apply their methods to the investigation of diseases of the skin. It is the purpose of this paper to present the results of some of these studies, especially those dealing with the influence of the weather on cutaneous disease.

The first dermatosis studied was generalized scleroderma of the type beginning with symptoms of Raynaud's disease, which occurred in a woman 27 years of age. Chiefly because of the high calcium and low potassium content of the serum, the case was regarded as an example of sympathicotonia in which abnormal tone of the tissue is due to hyperfunction of the sympathetic nervous system. Studies of such vagotonic diseases as urticaria and eczema made it seem possible to catalog disease entities as sympathicotonic or vagotonic, depending on which component of the autonomic nervous system was functionally predominant.

Later this precocious conception was rudely upset by the discovery of differences in potassium, calcium and cholesterol values, the time required for blistering and the permeability of the capillaries in the same patients at different seasons and times of the day. The patient with scleroderma, for instance, showed a higher cholesterol content of the blood and tissues and lower p_H values during the premenstrual periods than at other times. The ingestion of a meal, an intercurrent infection or an emotional shock caused marked fluctuations in the p_H values and leukocyte count. Thus I became impressed with the fact that various environmental factors influence the tone of the tissues. By observing normal and sick persons over a long period Petersen [3] demonstrated that the physiologic processes of the body are in a constant state of flux, varying in rate and amplitude from one minute to another. Comprehension of this fact will prevent investigators from attaching much weight to isolated analyses of the calcium content and p_H of the tissues.

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1. Zondek, S. G.: Die Elektrolyte, Berlin, Julius Springer, 1927.

2. Petersen, W. F.: The Skin Reactions, Blood Chemistry and Physical Status of "Normal" Men and of Clinical Patients, Arch. Path. **9**:151 (Jan., pt. 1) 1930.

3. Petersen, W. F., and Milliken, M. E.: The Patient and the Weather, Ann Arbor, Mich., Edwards Brothers, Inc., 1934.

Furthermore, it was determined that similar biologic reactions occurred in all of the patients on the same days. The type of reaction was conditioned by the individual constitution and the degree of instability of the autonomic nervous system, for the persons with a disturbance of the vegetative nervous system showed greater variation from normal than the person whose vegetative system was stable.

When the meteorogram was correlated with clinical symptoms and results of analyses of the blood and tissues, it was found that most persons react in the same way to changes in temperature and barometric pressure. During a polar infall, when the temperature drops and the barometric pressure rises, the most striking phenomenon is vascular spasm. The blood pressure increases and the tissues supplied by the blood vessels gradually become more acid. The capillaries are stimulated by the accumulation of carbon dioxide, and tissue inactivity rapidly passes over to anoxemic stimulation. Munk [4] recently demonstrated that temperature changes induce alterations in the electrical potential of the skin.

A tropical front is characterized by an influx of light, warm air, and the temperature rises while the barometric pressure falls. The functional response of the body is opposite to that induced by a polar infall. Between these extremes of reactivity occur countless physiologic variations, but when the bounds of functional capability are passed a return to normality is impossible and symptoms of disease become manifest.

In a previous contribution [5] I showed that the blood and oxygen supply of the skin is frequently inadequate to meet the demands placed on it. This deficiency is chiefly due to the fact that the blood vessels of the skin are largely terminal in type. The life of a hair structure, for instance, is entirely dependent on the blood supply of a single vessel.

The investigations of Scolari [6] on the capillaries of the skin substantiate my findings as to the inadequacy of the cutaneous blood supply. Scolari stated that the speed of circulation through the blood vessels of the skin may be alternately increased and diminished and that grave injury to the tissues results whenever the blood supply is diminished. He ascribed stasis with anoxemia to a colloidochemical phenomenon referable to disturbance of the equilibrium of the plasma, which when it appears in the peripheral vessels has an important effect in precipitating cutaneous symptoms. He concluded that the mechanism of stasis is not wholly clear.

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4. Munk, F.: Deutsche med. Wchnschr. **60**:1619 (Oct. 26) 1934.

5. Schmidt, F. R.: Blood and Oxygen Supply of the Skin, Arch. Dermat. & Syph. **32**:576 (Oct.) 1935.

6. Scolari, E. G.: Gior. ital. di dermat. e sif. **74**:1117 (Oct.) 1933.

Studies on the chemistry of the skin under normal and pathologic conditions have led me to lay chief emphasis on the alternating rhythm of vascular spasm and dilatation in the production of dysfunction and disease. Plasma stasis may thus be satisfactorily explained.

A number of environmental factors may act singly or in association to precipitate vascular spasm. Such factors are trauma, fright, anger, the weather, dysfunction of the endocrine glands (i. e., the onset of menstruation, thyroid disturbance, etc.), an infection or a specific allergen. Of these, the weather is most certain to produce spasm with anoxemia. A few dermatoses will illustrate the clearcut relationship of meteorological events and the precipitation of cutaneous symptoms.

ALOPECIA AREATA

Two cases of alopecia areata, chosen from thirty-one investigated, are presented with accompanying meteorograms.

CASE 1.—D. S., a girl 12 years of age, had had bald spots on the scalp for two weeks, the onset occurring on March 29, 1924.

The meteorogram (fig. *A*) indicates that the episode began with a sudden upturn of barometric pressure and fall in temperature, a typical polar infall.

In these graphs the dotted line indicates the mean temperature of the day in degrees Fahrenheit. The heavy solid line indicates the barographic record in inches.

CASE 2.—R. L., a man 28 years of age, received a blow on the head from running into a pipe on Sept. 12, 1933. Exactly two weeks later the hair began to fall out at the place where the injury had occurred.

Figure *B* shows that the injury occurred at the time of a polar infall but that the alopecia did not develop until the severe polar infall of Sept. 27, 1933. In patients in the hospital at the same time suffering from gastric ulcer and disorders of the eyes and ears, clinical episodes occurred on September 26.

The history of case 2 is characteristic, local trauma being followed by alopecia areata at a later date. Evidently the nerves and blood vessels of the region were altered by trauma and became unduly responsive. To the succeeding meteorological changes they responded selectively by an unusual dilatation and a correspondingly greater spasm.

HERPES ZOSTER

CASE 3.—D. G., a woman aged 32, first noticed a small blister on her right side on July 20, 1933. One week later a typical zoster had developed (fig. *C*).

CASE 4.—F. T., a man aged 56, noticed one small red spot on his forehead on Oct. 14, 1934. I saw the patient on October 16, at which time frank zoster had developed.

Figure *D* shows that the onset of the eruption coincided exactly with the beginning of a severe meteorological change.

CASE 5.—E. G., a woman aged 34, first noticed an eruption on her leg on June 28, 1934. She had had headache and severe pain in the back for three days preceding the appearance of the eruption (fig. *E*).

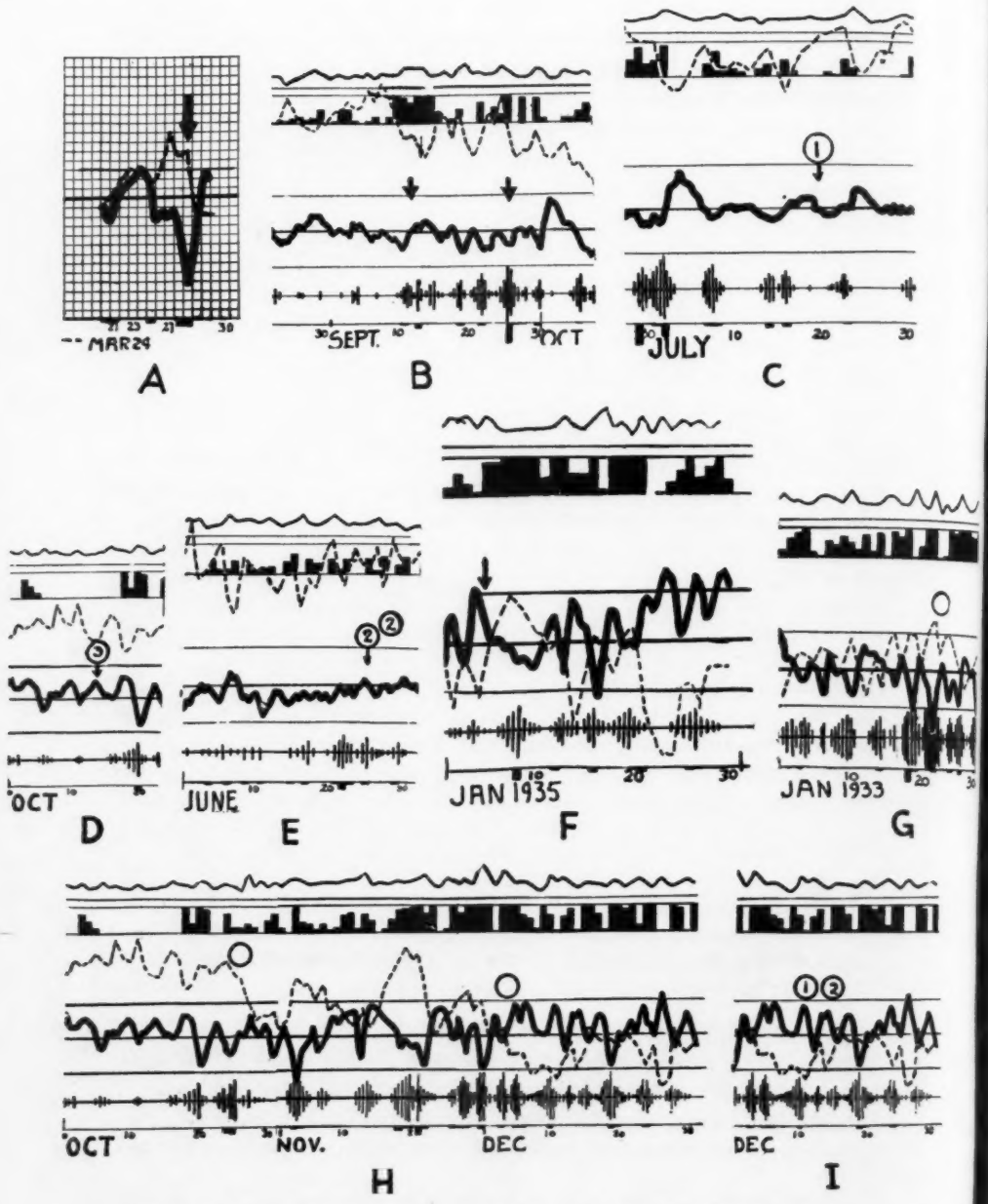

Fig. 1.—Curves showing weather conditions at the time of onset of the condition in each of the cases described in the paper. The dotted line indicates the mean daily temperature, and the heavy line indicates the barometric pressure in inches.

PSORIASIS AND GASTRIC ULCER

CASE 6.—K. G., a white man aged 42, had suffered from psoriasis and ulcer for many years. At times there was considerable itching. Early in the morning of Jan. 5, 1935, he was awakened by a severe cramp with abdominal distention. He had not deviated from his usual simple diet. During the next forty-eight hours the psoriasis became markedly worse.

Figure *E* shows that the clinical episode occurred at the very onset of a severe meteorological change.

The association of peptic ulcer and cutaneous diseases was noted by Neumann,[7] Lortat-Jacob,[8] G. Bergman [9] and others. My case coincides with that of Konjetzny,[10] who in 1933 reported the case of a woman suffering from psoriasis and gastric ulcer with the remark that "each exacerbation of the ulcer was accompanied by a flare-up of psoriasis." He pointed to the frequent association of ulcer and cutaneous diseases, particularly those accompanied by itching, but he did not assign a cause for the precipitation of attacks, although he said that most of the patients were vasoneurotic. This statement corroborates the hypothesis which I have advanced in this paper, as do the studies by which O. Mueller [11] demonstrated that vascular spasm in vasoneurotic persons leads to dysfunction and necrosis of the tissues of the stomach and skin. He based his conclusions on studies of the capillaries of the stomach and skin of his patients, which showed that the capillaries are characterized by tortuosity and irregularity of shape, number and size.

PITYRIASIS ROSEA

CASE 7.—H. A., a woman aged 35, first noticed spots on her body on Jan. 23, 1933. One week later the eruption had spread over the body (fig. *G*).

CASE 8.—H. A., a man aged 52, first noticed spots on his body on Oct. 26, 1934. The circle in figure *H* placed above the beginning of the long polar infall in October indicates the date of onset of the dermatosis.

CASE 9.—L. T., a boy aged 11 years, noticed a spot on his chest on Dec. 4, 1934, and within the next six or seven days the eruption had spread a good deal (*H* of the figure).

ULCUS VULVAE ACUTUM

CASE 10.—V. T., a girl aged 19, was taken acutely sick with sore throat, fever and a cough (*1* in fig. *I*). Four days later, on Dec. 15, 1934 (*2* in fig. *J*), she had a sharp pain in the vulva on urination and on examination found two sores. I examined the patient two days later and observed one oval, sharply demarcated ulcer about 2 cm. in diameter on the inner side of the left labium majus pudendi with a smaller ulcer on the surface of the opposing labium. A smear made from

7. Neumann: Arch. f. Dermat. u. Syph. **48**:353, 1899.
8. Lortat-Jacob, L.: Presse méd. **33**:1699 (Dec. 26) 1925.
9. Bergman, G.: Wien. klin. Wchnschr. **47**:945 (July 27) 1934.
10. Konjetzny, G. E.: Wien. klin. Wchnschr. **46**:451 (April 14) 1933.
11. Mueller, O., cited by Bergman.[9]

these ulcers disclosed many gram-positive cocci. Cultures proved these to be staphylococci (Staphylococcus albus), pseudodiphtheria bacilli and a gram-positive strain of Bacillus crassus, which have been definitely established as identical with Doederlein's vaginal bacilli.

It is well known that such ulcers appear seasonally, especially in the spring and at other times of great meteorological change. Scherber [12] recently reemphasized the fallacy of ascribing the ulcers to B. crassus, first described by himself and Lipschuetz. Undoubtedly any one of various environmental factors may prepare the mucous membranes of the vulva and mouth for their eventual destruction by different microorganisms.

COMMENT AND CONCLUSION

Darier [13] recently expressed the view that certain dermatoses are the result of an interplay between the person's constitution and environment. He placed dermatitis herpetiformis in this group, believing that any one of several environmental factors can precipitate the disease in a person who is predisposed to it. This is in accord with my findings, as previously stated, that the type of biologic and cutaneous reaction is conditioned by the individual constitution and degree of instability of the autonomic nervous system. The environmental factors capable of precipitating cutaneous symptoms are numerous, and it appears that the weather is an important one.

12. Scherber, G.: Dermat. Wchnschr. **99**:1553 (Dec. 1) 1934.
13. Darier, J., and Tzanck, A.: Dermat. Wchnschr. **100**:73 (Jan. 19) 1935.

USE OF AUTOGENOUS FUNGUS EXTRACTS IN THE TREATMENT OF MYCOTIC INFECTIONS

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Literature on the subject of mycotic infections has dealt largely with the extent of their distribution among persons and on their chemical prophylaxis and therapeusis. More recently, the relation of allergy to the manifestations of the diseases produced by various fungi has been given considerable thought. As a result of this association, a new mode of therapy, namely, the use of desensitization by means of extracts, suggested itself and has been reported on from time to time. The late Bruno Bloch, of Switzerland, and his followers in this country have been largely responsible for stimulating interest along this line of approach. As a result of closer cooperation between the bacteriologist and the clinician, numerous conditions that were relegated to the heterogenous group of "eczema" have been definitely identified as belonging to one of the fungous infections. This is especially true of those cases in which vesicular eruptions on the hands were considered as pompholyx or as dyshidrosis of the type described by Tilbury Fox.

In this connection Sulzberger and Wise [1] explained that secondary vesicular involvement of the hands following mycotic infection of some other part of the body, particularly of the feet, is due solely to an allergic state, because repeated cultures made by them of these vesicular lesions yielded negative results. The reason for predilection of the hands for secondary manifestations was not explained by the authors. However, Peck [2] suggested that the keratinization found in the skin of the hands predisposed them to a greater degree of sensitization, and thus he attempted to explain away Sabouraud's [3] criticism of poor technic in the culturing of the fungi. Though we agree that fungi cause a state of sensitization, our bacteriologic observations of the vesicular eruptions on the hands would argue against their being due solely to secondary allergic phenomena. We were able to culture fungi from the scales of these areas in thirty-one cases. The inordinate itching associated with mycotic infections brings the hands into direct contact with the infected

From the William H. Singer Memorial Research Laboratory of the Allegheny General Hospital.

1. Sulzberger, M. B., and Wise, Fred: Ringworm and Trichophytin: Newer Developments, Including Practical and Theoretical Considerations, J. A. M. A. **99**:1759 (Nov. 19) 1932.

2. Peck, S. M.: Epidermophytosis of Feet and Epidermophytids of Hands: Clinical, Histologic, Cultural and Experimental Studies, Arch. Dermat. & Syph. **22**:40 (July) 1930.

3. Sabouraud, quoted by Peck.[2]

parts through scratching. Thus it would seem that infection of the hands is likely if conditions are favorable to the growth of the organism. From practically all the conditions which we have studied, including dermatitis of the hands, feet and body, we have been able to obtain a fungus. The failures were few and were possibly due to our having poor specimens for culture.

We extended our studies to include the treatment of a patient with pulmonary aspergillosis, one with perennial rhinitis and several children with microsporon infections of the scalp. The latter group will be reported on in a subsequent publication.

METHODS

Culture Mediums.—For the isolation of the fungi we used the medium which Corper [4] recommended for the cultivation of tubercle bacilli: pieces of potato soaked in a 1:70,000 solution of crystal violet and kept moist by a small amount of glycerin broth. Fungi grow readily on this medium, while other organisms are retarded by the dye. Agar containing 2 per cent maltose was used for studying colony formation.

Preparation of Extract.—The therapeutic preparations of Bloch [5] and others were based on the assumption that the fungi produce a toxin in old broth cultures. The organisms were allowed to grow in broth for several months, and then the filtered medium was used. We tried such preparations, but with indifferent success. The extract we used includes not only the endotoxin of the vegetative forms of fungi but some particulate portions of the bodies which we believe are desirable in stimulating immunity.

A pure culture of the fungus is inoculated into a tube of plain broth and allowed to grow at room temperature for a week or ten days. The puffball or pellicle growth is then removed with a platinum wire and washed in several changes of saline solution. The growth is then placed in a mortar with only the drop of saline solution adhering to it and ground for thirty minutes. The moist paste is then taken up in 5 cc. of a 0.5 per cent solution of phenol in 0.85 per cent solution of sodium chloride and heated for thirty minutes at 65 C. The suspension is shaken and allowed to stand until the coarser particles have settled, leaving a smooth turbid supernatant. This supernatant is added to phenolized solution of sodium chloride until a faint opalescence, about equal to a bacterial suspension containing 100,000,000 bacteria per cubic centimeter, results. It is then filled into ampules and tested for sterility. Such a preparation can be used either for cutaneous tests or for desensitization.

We have used the following strains in our stock extract:

Epidermophyton niveum from the skin
Microsporon villousum from the scalp
Microsporon Audouini from the scalp
Trichophyton niveum from the feet
Two unidentified strains from the scalp.

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4. Corper, H. J.: Certified Diagnosis of Tuberculosis: Practical Evaluation of New Method for Cultivating Tubercle Bacilli for Diagnostic Purposes, J. A. M. A. **91**:371 (Aug. 11) 1928.

5. Bloch and Massini: Studien über Immunität und Ueberempfindlichkeit bei Hyphomyzetenerkrankungen, Ztschr. f. Hyg. u. Infektionskr. **62**:68, 1909.

In a polyvalent extract the same amount of each strain is used, and all are ground together. It is quite possible that a better selection of strains could be made on the basis of more extensive experience. It is also probable that for use in tropical regions an entirely different group of fungi should be employed. However, for the cases of dermatophytosis of the scalp, feet and hands which we have encountered, our combination of strains has been effective.

DIAGNOSIS OF MYCOTIC INFECTIONS

The use of clinical criteria alone in making a diagnosis of mycotic infections accounts for the erroneously high percentage of such infections. Two methods may be employed in arriving at a diagnosis: growing the offending fungus on artificial mediums and testing the skin of the patient with a stock extract that contains several of the commoner fungi. It is readily apparent that demonstration of the fungus by growth is the only positive method. But, cutaneous testing is more easily accomplished and hence more feasible for the practitioner who does not have the facilities of a laboratory readily accessible.

The cutaneous test practiced by us consisted of injecting 0.05 cc. of a stock extract intradermally to produce a small wheal. The site of injection was observed at intervals of between twelve and thirty-six hours, when the reaction usually reached its greatest height. A positive reaction consists of an area of erythema and infiltration. Brown pigmentation often remains at the site of injection for several days after the reaction has subsided. In this respect it closely resembles a positive cutaneous reaction to tuberculin. It is interesting to note that Amberg[6] in 1910 drew a close analogy between the cutaneous reactions to tuberculin and those to trichophytin.

While it is not the rule, it is possible for persons not infected either with Trichophyton or with Monilia to give a positive cutaneous reaction to the extracts of these fungi. Hence, a certain degree of error results when such persons are considered to be infected with fungi in the absence of proof obtained by culture. Conversely, it does not follow that in all cases fungous infection produces a state of demonstrable sensitization. It was fairly common in our series for a mycotic infection to be present without a positive cutaneous reaction to the autogenous extract. It may be that in such cases the skin test dose is below that necessary to elicit response of the tissue to the injected material. Regarding this observation, it has further been our experience occasionally to observe a local cutaneous reaction to an injected autogenous extract with larger therapeutic doses when no reaction had been elicited with a skin test dose of 0.05 cc. In cases in which no reaction was observed either as a result of testing or during treatment, a possible explanation presents itself in the well known occurrence of localized allergic changes in the skin about

6. Amberg, Samuel: The Cutaneous Trichophyton Reaction, J. Exper. Med. **12**:435, 1910.

infected sites in the absence of generalized allergy. This would explain negative reactions after the use of autogenous extracts in a few cases in which the lesions healed after the use of the vaccine. Such exceptions emphasize the preference of making a culture when possible rather than trusting to cutaneous tests alone.

TREATMENT

Regulation of Doses.—It is of the utmost importance to regulate the dose carefully and to realize that the only index to the size of the dose and to the frequency of administration is the patient's reaction. No hard and fast rules can be formulated for standardization of dosage. We have found it advisable to begin with a skin test dose of 0.05 cc., which is injected intradermally. Subsequent injections are given at intervals of from five to seven days, provided that all signs of local reaction to the preceding injection have disappeared. The amount injected is increased by 0.05 cc. each time. If a marked local reaction has occurred, the succeeding dose is of the same amount as the preceding one. This is continued until no local or focal reaction occurs. Thereafter, the next amount is increased by 0.05 cc. until a dose of 0.4 cc. is reached. If the condition has not entirely cleared up by this time, the dose is maintained at 0.4 cc. In some instances in which we found the patient hypersensitive to the smallest dose, the extract was further diluted with phenolized solution of sodium chloride until a suspension was reached which produced only a mild local reaction.

Several patients improved for a time and then failed to make further progress. New cultures made from the scales of the lesions at this time yielded a different fungus from that originally obtained. An extract was then made from the new culture, and its administration led to rapid disappearance of the lesions. Thus a supposedly refractory group of patients were found to be suffering either from a mixed mycotic infection or from a superimposed infection. In either event these cases reemphasize the specificity that may exist in some instances. These are the ones in which autogenous extracts were definitely indicated. Kerr, Pascher and Sulzberger [7] found a group of six cases in which the lesions did not clear up by the use of a trichophyton extract, but when a monilia extract was used in addition some patients improved and others were cured. These authors used cutaneous tests alone for diagnosis. It is to be regretted that they did not make cultures of the lesions in order to determine definitely whether or not the offending fungus was of the Monilia group.

We were able to clear up the vesicular eruptions on the hands, known as dermatophytids, promptly in all cases. There were several cases in

7. Kerr, Phyllis S.; Pascher, Frances, and Sulzberger, M. B.: Monilia and Trichophyton Extracts: Their Combined Use in Eczematous Ringworm (Dermatophytosis and Dermatophytids), J. Allergy **5**:288 (March) 1934.

which deep-seated lesions on the feet persisted; it was in these cases that subsequent cultures revealed a coexistent unrecognized fungus and in which a newly prepared autogenous extract hastened complete healing.

In several cases numerous small papules the size of a pinhead appeared on the hands and arms and in one case, generally over the body after the second or third intracutaneous injection was administered. Such provocative lesions are, in our opinion, the ones to which the term "ids" or secondary lesions should be applied. These allergic lesions were accompanied by itching and ultimately became vesicular. When such lesions were elicited, desensitizing of the skin was accomplished by returning to the original dose of 0.05 cc. or by using a diluted extract. The diminished dose was then maintained consistently until all allergic lesions had disappeared. Even then caution was exercised in increasing the dose in such cases in order to avoid a recurrence of the hypersensitive state.

Undesirable Effects of Overdoses.—At the beginning of our work, before the harmful possibilities of overdosage had been realized, we experienced interesting unexpected reactions. The following case is an illustration of this.

Mrs. F., who suffered from pruritus ani caused by an infection with Alternaria, was entirely relieved of symptoms after a few injections of small amounts of autogenous extract. As a final treatment, 2.5 cc. of extract was given. Within a few hours the patient experienced a marked itching at the focal site followed by a marked vesicular eruption, weeping eczema and a dermatitis which lasted six weeks. After prolonged treatment with carefully regulated doses she was cured. For a long time the hypersensitive stage produced in her by the overdose prevented us from administering over 0.3 cc. without securing a marked focal reaction.

Visceral Mycoses.—The sensitizing effect of fungi is not limited to cutaneous reactions, since cases of asthma, pulmonary mycoses, urticaria and hay fever have been reported due to fungi. Here again close bacteriologic cooperation is essential in both diagnosis and treatment.

In our series, evidence of the specificity of autogenous fungus extracts in the treatment of visceral mycosis was observed in a case [8] of pulmonary aspergillosis.

Mrs. M. first consulted her doctor on May 22, 1915, with a previous diagnosis of pulmonary tuberculosis. After two years of institutional care in New Mexico, the patient was greatly improved and remained well for several years. On Aug. 20, 1928, she returned with slight fever, loss of weight and slight cough. Examination revealed dulness, bronchial breathing and voice and râles over the base of the left lung. Roentgen examination showed cloudiness at the area corresponding to the position of the physical signs. In June 1931 the area at the base of the left lung had increased considerably in size, and the symptoms were exaggerated. At this time culture of the patient's sputum was productive of a

8. This case was observed in collaboration with Dr. J. P. McKelvy, who gave us permission to report the case.

growth of Aspergillus fumigatus. Treatment with an autogenous extract was begun on June 10, 1931. Eight small intradermal doses, the maximum of which was 0.3 cc., were administered at five day intervals. Thereafter, subdermal doses, beginning with 0.5 cc. and increasing to 2 cc., were given. The course of the injections terminated on Oct. 5, 1931. Cultures of the sputum made on Oct. 10, Nov. 9 and Dec. 31, 1931, and May 24, 1932, were all negative for the fungus. A note on the patient's progress on Feb. 8, 1932, stated: "The patient looks and feels much better; the cough has disappeared; there is marked improvement in the signs at the base of the left lung. The voice and breath sounds are normal; the patient has gained 5 pounds (2.2 Kg.) in weight." Roentgenograms taken on Jan. 13, 1933, revealed improvement in the roentgen shadows as compared to the first plates.

Bakst, Hazard and Foley [9] reported on the successful use of vaccines in the treatment of two patients with primary pulmonary moniliasis. The treatment was supplemented by the use of iodides, so that proper evaluation of the vaccine was necessarily interfered with.

We studied a case of perennial rhinitis in which Monilia was grown on cultures from the tonsils. The patient was greatly benefited by intracutaneous injections of an autogenous fungus extract. Flood [10] found that 14 per cent of a group of fifty-five asthmatic patients gave positive cutaneous reactions to air-borne fungi. An asthmatic attack was produced in one of these patients by spraying the nose and throat with a filtrate of Mucor plumbus, one of the fungi to which the patient gave a positive cutaneous reaction.

Analysis of Cases.—In attempting to determine the more common pathogenic fungi associated with the cases listed in the table, we were confronted with the difficulty of proper identification owing to the wide variety of data employed by various mycologists. As a result, eleven cases were not classified though autogenous extracts were made and treatment employed. It is interesting to observe that the generally accepted Trichophyton was not the chief offender in our series of cases but that Aspergillus was most often isolated (seventeen cases). Eleven cases were due to Trichophyton. Penicillium, Sporothrix and Mucor were isolated in several cases each. It is especially significant that Alternaria, ordinarily considered nonpathogenic, was obtained in three cases in pure culture. Treatment with autogenous extracts in these cases resulted in alleviation of symptoms and disappearance of the lesions. Twenty-three patients were treated with a polyvalent stock extract. Scales from all of these were examined microscopically for fungi, but cultures were not obtained. Nineteen were completely cured, while one showed no improvement. Three of these were definitely improved. Apparently, the polyvalent extract prepared according to our method is

9. Bakst, Henry J.; Hazard, J. Beach, and Foley, John A.: Pulmonary Moniliasis, J. A. M. A. **102**:1208 (April 14) 1934.

10. Flood, C. A.: Sensitivity to Dust Fungi in Patients with Asthma, J. A. M. A. **96**:2094 (June 20) 1931.

Tabulation of Data for a Series of Patients with Mycotic Infections Successfully Treated with Autogenous Extracts

Name	Age	Location of Lesion	Organism	Duration of Condition	Comment	Extract
M. B. P.	Adult	Leg	Aspergillus	1 yr.	Cured	
E. W.	Adult	Hands	Aspergillus	3 yr.	Improved	
G.	Adult	Hands	Aspergillus	6 mo.	Unimproved	
Gear.	Adult	Hands	Aspergillus	16 mo.	Cured	
V.	Adult	Hands	Aspergillus	2 yr.	Improved	
W.	Adult	Feet	Aspergillus	.....	Cured	
M.	Adult	Feet	Aspergillus	6 mo.	Cured	
L.	Adule	Hands	Aspergillus	1 yr.	Cured	
B.	Adult	Hands and feet	Aspergillus	1 yr.	Improved	
M.	Adult	Anus and nails	Aspergillus	2 yr.	Improved	
J. R.	Adult	Feet	Aspergillus	2 yr.	Much improved	
J.	Adult	Anus and feet	Aspergillus	.....	Cured	
C.	Adult	Feet and hands	Aspergillus	12 yr.	Cured	
J. M.	Adult	Hands	Aspergillus	6 yr.	Cured	
J. D.	Adult	Feet	Aspergillus	1 yr.	Cured	
J. K. H.	Adult	Hands and feet	A. glaucus, A. sulphurus	1 yr.	Cured	
R.	Adult	Feet	Trichophyton	3 yr.	Cured	
R. T.	Adult	Hands	T. album	2 yr.	Cured	
P. McG.	Child	Hands	T. rosaceum	6 mo.	Cured	
N.	Adult	Face and anus	Trichophyton	.....	Cured	
C.	Adult	Hands	Trichophyton	.....	Cured	
B. A. R.	Child	Face	Trichophyton	6 mo.	Cured	
Mrs. W.	Adult	Anus	Trichophyton	2 yr.	Cured	
Miss E.	Adult	Feet	Trichophyton	3 yr.	Unimproved	
Mrs. F.	Adult	Anus and nails	Alternaria	3 yr.	Cured	
R. M.	Adult	Legs	Alternaria	.....	Cured	
W. J. H.	Adult	Hands	Alternaria	.....	Cured	
Dr. S.	Adult	Feet	Epidermophyton	.....	Cured	
M.	Adult	Feet and anus	Epidermophyton	.....	Cured	
R.	Adult	Hands	Epidermophyton	.....	Cured	
Dr. M.	Adult	Hands and feet	Epidermophyton	.....	Much improved	
S. S. J.	Adult	Hands	Epidermophyton	.....	Cured	
J. K.	Adult	Hands and feet	Sporothrix	10 yr.	Cured	
T.	Adult	Hands	Sporothrix	1 yr.	Cured	
A.	Adult	Hands	Mucor	1½ yr.	Cured	
C.	Adult	Feet	Mucor	6 mo.	Cured	
H.	Adult	Anus	Penicillium	4 yr.	Cured	
B.	Adult	Feet and hands	Penicillium	3 yr.	Cured	
M.	Adult	Hands	Penicillium	1 yr.	Cured	
T. D.	Adult	Feet	Penicillium	.....	Cured	
R. T.	Adult	Feet	Unidentified	4 yr.	Cured	Stock
J.	Adult	Hands	Unidentified	3 yr.	Cured	Stock
McK.	Adult	Anus and vulva	Unidentified	2 yr.	Cured	Stock
C. K.	Adult	Face and hands	Unidentified	6 yr.	Cured	Stock
H. R.	Adult	Hands and feet	Unidentified	1 yr.	Cured	Stock
M. T.	Child	Hands	Unidentified	6 mo.	Cured	Stock
J. D.	Child	Hands, legs and body	Unidentified	8 yr.	Cured	Stock
H. L. W.	Adult	Hands	Unidentified	.....	Cured	Stock
M. E.	Adult	Hands	Unidentified	5 yr.	Cured	Stock
J. E. R.	Adult	Hands	Unidentified	2 yr.	Unimproved	Stock
S. S.	Adult	Face	No growth	.....	Unimproved	Stock
W. S.	Adult	Hands, face and neck	No growth	.....	Unimproved	Stock
W. D.	Adult	Hands	No growth	.....	Unimproved	Stock
N. F.	Adult	Hands	No growth	2 yr.	Cured	Stock
K. W.	Adult	Hands	No growth	2 yr.	Cured	Stock
R.	Adult	Hands	No growth	3 yr.	Improved	Stock
J. T.	Adult	Hands	No growth	1 yr.	Cured	Stock
D. A. G.	Adult	Anus	No growth	4 yr.	Cured	Stock
J. S.	Adult	Scrotum	No growth	15 yr.	Improved	Stock
D.	Adult	Hands	No growth	1 yr.	Much improved	Stock
M. D.	Adult	Hands and feet	No growth	1 yr.	Cured	Stock
Dr. B.	Adult	Hands	No growth	3 yr.	Cured	Stock
Dr. C.	Adult	Hands	No growth	6 mo.	Cured	Stock
Mrs. M.	Adult	Lungs	A. fumigatus	19 yr.	Cured	Autogenous
Mr. M.	Adult	Lungs and sinuses	A. fumigatus	.....	Unimproved	Autogenous
R. R.	Adult	Mucous membrane of nose and throat	Monilia	5 yr.	Greatly improved	Autogenous

efficacious and can be employed in cases in which an autogenous extract cannot be obtained.

It is probable that many of the common molds and yeasts abounding in nature are more pathogenic to man than has been generally recognized.

For example, we cultured a pink mold from a lesion of the scalp of one patient and also found it in some decayed wood of his automobile. The patient had a distinct recollection of having picked at the mold with his fingers, after which he passed his hand through his hair.

The length of time consumed in treatment varied considerably. The most rapid and spectacular response to the administration of a stock extract was that of Dr. C., whose lesions, consisting of small trichophytids of the hands, cleared completely after only two injections. Another patient, Mr. T., showed complete healing after eight intracutaneous injections of vaccine. On the other hand, the longest time which treatment was continued with ultimate success was that in the case of a child 10 years of age who had had lesions over the body, arms and legs since he was 2 months old. Cutaneous testing and cultures led to a diagnosis of an unidentified fungous infection. Treatment in this case was continued for about fourteen months, after which time all the lesions were completely gone. This was the first time since infancy that the patient has been free from the scaling eruption.

We found that the patients who had received roentgen therapy without benefit were far more resistant to treatment than those who had not been treated by irradiation. This may be explained on one of two theories. Either the patients who received roentgen irradiation without benefit were primarily so resistant to treatment that they presented a natural resistance to the use of vaccines or the administration of the roentgen radiation produced sufficient drying of the skin to interfere seriously with cutaneous circulation and hence to interfere with the efficacy of the vaccine. We are inclined to believe that the latter is the explanation, as patients whose condition resisted all forms of fungicides but who had not received roentgen therapy responded readily to the vaccines.

CONCLUSIONS

A series of patients with mycotic infections successfully treated with autogenous extracts is reported.

A method of preparing autogenous fungus extracts for the treatment of mycotic infections is described.

A stock extract may be employed with success in cases in which an autogenous extract is unobtainable.

Intradermal injections of the fungus vaccine should be adjusted to the person's reaction.

A case of pulmonary mycotic infection was successfully treated with an autogenous vaccine.

Clinical and bacteriologic cures obtained by treatment with fungus vaccine recommend it as a means of therapy for refractory dermatomycoses.

VALUE OF INTRADERMAL INJECTION OF SERUM AS A DIAGNOSTIC TEST FOR LYMPHOGRANULOMA INGUINALE

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In a recent article Reiss[1] stated that blood serum taken from patients known to have lymphogranuloma inguinale produced an intradermal reaction comparable to that in the Frei test. The substitution of blood serum for Frei antigen would facilitate the more widespread use of intradermal tests for lymphogranuloma inguinale, which now frequently cannot be made because of the difficulty of obtaining Frei antigen.

A series of intradermal tests with blood serum was carried out in cases of recognized lymphogranuloma inguinale, in order to verify the results reported by Reiss.

TECHNIC

Seven intradermal injections of 0.1 cc. each were made in the forearm of the only five patients with lymphogranuloma inguinale that were available. Each of these patients had previously shown a distinctly positive reaction to the Frei test. As control tests, similar injections were given to five patients having no clinical evidence of lymphogranuloma inguinale, each of whom presented a negative reaction to the Frei test. The results were further controlled in injections of physiologic solution of sodium chloride and normal blood serum.

On each patient tests were made with serums obtained from two patients known to have lymphogranuloma inguinale, Frei antigen and mixtures of equal parts of Frei antigen and each of the two serums.

Sufficient phenol was added as a preservative to each of these test substances to give an end-concentration of 0.5 per cent. The saline solution and the normal blood serum, also containing phenol, served as controls for possible reactions to the phenol. All tests were made within two weeks after preparation of the materials in order to insure no loss of potency. Before use, each substance was tested for sterility and then kept in an ice box.

One serum was obtained from a patient with active lymphogranuloma inguinale of three weeks' duration, who presented fluctuant inguinal glands, the size of an egg, on the right side; the other from a patient with lymphogranuloma inguinale

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Studies and Contributions from the Department of Dermatology and Syphilology, the University of Michigan Medical School, service of Dr. Udo J. Wile.

1. Reiss, Frederick: Ueber eine neue immunbiologische Reaktion zur Diagnose der Lymphogranulomatosis inguinalis, Dermat. Wchnschr. **99**:1203 (Sept. 15) 1934; A New Immunologic Reaction for the Diagnosis of Lymphogranuloma Inguinale, Arch. Dermat. & Syph. **31**:215 (Feb.) 1935.

of twelve years' duration and resultant stricture of the rectum. It was thought that the duration of the disease might influence the antigenic properties of the serum.

RESULTS

Observations made twenty-four and forty-eight hours after intradermal injection showed that positive reactions were slightly more pronounced at the end of forty-eight hours.

None of the five patients used as controls who reacted negatively to the Frei tests gave a positive reaction to the intradermal tests, except one, who showed mild erythema at the site of injection of the normal serum.

All of the five patients with lymphogranuloma inguinale showed positive reactions to the Frei antigen, and the mixtures of serum and Frei antigen produced reactions indistinguishable from those to the Frei antigen alone. The serums from the patients with lymphogranuloma inguinale caused no reaction, except slight erythema in one patient with active lymphogranuloma inguinale, produced by the serum from the patient with stricture of the rectum.

No reactions were obtained from the injections of physiologic solution of sodium chloride and normal blood serum used as controls.

COMMENT

The single slight reaction to normal serum observed in a control patient can best be explained as a specific reaction of that patient to the foreign protein of the particular serum.

Of much more interest is the fact that of the five patients giving positive reactions to the Frei test, only one reacted to the intradermal injection of serum from a patient with lymphogranuloma inguinale. Whether that one reaction, which was much less marked than that to the Frei test, was likewise due to a sensitivity to the serum injected or whether it was a specific reaction to an antigenic property resulting from lymphogranuloma inguinale is difficult to decide. In this regard, Saenz [2] mentioned that the skin of patients receiving roentgen therapy may show an increased allergic reaction. The patient with active lymphogranuloma inguinale had been receiving roentgen therapy over the inguinal regions. Possibly he therefore possessed sufficiently increased cutaneous sensitization to react to the serum of another patient with lymphogranuloma inguinale.

No difference was noted between the reactions obtained to the Frei antigen and those to the mixture of Frei antigen and serum from a patient with lymphogranuloma inguinale. In view of the fact that two

2. Saenz, Braulio: Unusual Form of Allergic Cutaneous Reaction in Lymphogranulomatosis Inguinalis, Arch. Dermat. & Syph. **31**:348 (March) 1935.

serums were used, one from a patient with active disease and the other from a person with a condition of long standing (twelve years), with no difference in the extent or type of the reactions, one may conclude that serum from a patient with lymphogranuloma inguinale does not contain properties which counteract the reactivity to Frei antigen or any which cause an intradermal reaction when serum is used alone.

SUMMARY

Five patients with lymphogranuloma inguinale showing positive reactions to Frei antigen were tested under adequate conditions of control with intradermal injections of serum from patients known to have lymphogranuloma inguinale.

The mixture of Frei antigen and serum from a patient with lymphogranuloma inguinale produced the same cutaneous reaction as that to Frei antigen alone.

The intradermal injection of serum from patients with lymphogranuloma inguinale into patients showing positive reactions to Frei antigen caused no reaction, with one doubtful exception.

Therefore, it seems that the substitution of serum for Frei antigen is not satisfactory as a diagnostic procedure in cases of lymphogranuloma inguinale.

Clinical Notes

DERMATITIS HERPETIFORMIS ASSOCIATED WITH FOOD ALLERGY

Report of a Case

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Dermatitis herpetiformis is considered by most dermatologists to be of unknown etiology and to occur most frequently in nervous and neurotic persons. Various authors have speculated as to the cause of dermatitis herpetiformis, and a few have suggested anaphylaxis as an etiologic factor. Others have agreed that toxic and psychic factors are present.

In this country Sutton [1] described a case in a child, which developed after the child had been given cow's milk. The mother noticed "mosquito bites" on the child's legs and thighs. Vesicles soon formed, and later pigmented spots appeared. There were subsequent attacks. The child responded to treatment with thyroid extract.

Schwartz [2] noted a disorder of protein metabolism in this condition. He emphasized the eosinophilia and expressed the opinion that not only should cutaneous tests be given to find the offending protein but a clinical trial with foods should be made as well.

Squallaci [3] reported a case of associated herpes zoster, eczema and dermatitis herpetiformis.

REPORT OF CASE

The patient is a woman, 33 years of age, the wife of a physician. She is in excellent health and is not particularly nervous.

The family history of allergy is significant. The patient's mother had attacks of sneezing on contact with certain flowers, and she was sensitive to narcotics. The mother's sister had an idiosyncrasy for eggs, fish and strawberries; her half-sister had hay fever, and her brother had nausea and vomited after drinking cow's milk. The child and grandchild of the sister had angioneurotic edema and eczema, respectively. The patient's father in infancy did not tolerate cow's milk and was fed goat's milk.

The patient has a sister and five brothers. The sister is sensitive to eggs, milk, beef, fish and pork, and develops urticarial, vesicular or pustular and aphthous lesions after the ingestion of small amounts of these foods. She is sensitive to all narcotics. One of the brothers is sensitive to coal-tar products. This is manifested by cutaneous eruptions. Three brothers do not show symptoms of allergy, but one child of each of two brothers has eczema and urticaria, respectively.

In childhood the patient was not able to eat shell-fish, as this produced diarrhea and cramps. She was well and ate all foods until 1929, when she contracted impetigo contagiosa from a child. This was much aggravated by the application of ammoniated mercury ointment, and a severe dermatitis developed. Red blood

1. Sutton, R. L.: Am. J. M. Sc. **140**:727 (Nov.) 1910.
2. Schwartz, Hans T.: J. Cutan. Dis. **31**:994, 1913.
3. Squallaci, R.: Riv. san. siciliana **20**:412 (March 15) 1932.

cells and casts appeared in the urine, and the patient was quite ill. Examination of the blood at this time disclosed normal values for nonprotein nitrogen and sugar.

During convalescence, recurrent groups of vesicles appeared on various parts of the body, including the conjunctiva. The appearance was preceded by severe itching, burning and pain. At this time, after healing they did not leave pigmented spots. Because of the allergic history it was suggested that the patient have tests for sensitivity to foods. These were carried out by the scratch method and caused no reaction. Because of the persistence of the symptoms the patient was advised to eat only vegetables, toast and fruit for three months. During this time the symptoms cleared up completely. She began to add new foods, one by one, allowing from five to six days to elapse between each addition to the diet, and found that the following foods caused herpetiform lesions: eggs, beef, cheese and fish. Milk, strawberries and corn caused urticaria. Alligator pear and gin caused nausea and vomiting. Thirty-six hours after the ingestion of the foods there were severe itching, burning and pain along the course of a sensory nerve, and then the papular, urticarial and vesicular lesions appeared. These became pustular in a few days. On one occasion the lesions were hemorrhagic. In the past few years the lesions have been followed by groups of pigmented spots, which may be seen on the leg, near the knee, on the wrist and in the sacral region. In this last-mentioned area annoying cracks and fissures were present during one attack. It is of interest that the merest trace of egg or beef will bring out these reactions, the patient being unable to put her hands on raw egg white or beef. Lesions have occurred twice on the left cornea in the form of vesicles, once healing spontaneously and once requiring surgical intervention.

Until 1935 the case was considered one of food allergy associated with herpes. The patient was vaccinated in the left deltoid region in the hope of producing some immunity to the herpes virus. The vaccination did not cause a reaction, and herpetiform lesions appeared in thirty-six hours on the left arm and shoulder, the back of the neck and the left side of the face, preceded by the usual symptoms. It was suggested that enough cow serum was scratched into the skin to produce an allergic reaction.

I was requested to make a test on the patient by the transfer method of Prausnitz and Küstner. This was done with the husband as the recipient. The sites were sensitized in the usual manner with 0.2 cc. of the patient's serum and were tested intradermally forty-eight hours later with foods known to cause reactions and with other foods. A reaction did not develop. It is of interest that the patient's sister was tested intradermally and gave no reaction to the foods which cause her lesions. The sisters have a close physical resemblance and have clinically identical sensitiveness to food and drugs.

A patch test for iodides was not permitted, as the patient said that she is sensitive to all drugs, with urticaria developing after the ingestion of acetylsalicylic acid, phenobarbitol and ipral calcium, with nausea and vomiting from narcotics and with dermatitis from mercury and possibly from other metals.

A blood count in June 1935 revealed: hemoglobin content, 88 per cent; color index, 0.9; red cells, 4,400,000, and white cells, 6,150, with lymphocytes 30 per cent, large mononuclears 5 per cent, eosinophils 2 per cent, neutrophils 63 per cent, stab forms 3 per cent and mature forms 60 per cent. A chemical analysis of the blood gave normal results. There was slight achromia. The urine was normal. The Wassermann reaction was negative.

Physical examination revealed the patient to be in excellent condition.

Until this time a diagnosis of dermatitis herpetiformis had not been definitely considered. The patient was examined by Dr. Marion B. Sulzberger, who stated

that the clinical appearance of the polymorphic eruption, the grouped pigmentation and the history suggest the diagnosis of dermatitis herpetiformis. The patient is to receive an injection of 15 cc. of her own blood into the gluteal muscles once a week for twenty weeks. This treatment was used by Watrin [4] in a similar case, in which nine injections were given, and the eruption failed to reappear in five months.

Since my observation of the patient there has been no opportunity to examine the fluid of the blisters to determine whether eosinophilia is present. The patient has been instructed to eat food prepared only in her own home by some one intelligent enough to understand the importance of avoiding the merest trace of offending foods.

NOTE.—Recently the inadvertent ingestion of iodized salt was followed by five groups of lesions on the mucous membranes.

COMMENT

I am reporting this case in the hope that it may be of some value in determining the etiology of this disease. The family history of allergy should be investigated, and the presence of other forms of allergy in the patient should be looked for. There is a possibility of there being shock tissues other than those commonly described in association with allergy, i. e., the skin and the mucous membranes. This may be the tissue of the ganglion cells, as they are also ectodermal derivatives. I have no theory as to the mechanism of the reaction, although I think that there are other mechanisms than the atopen-cell-reagin mechanism in allergic reactions.

745 Fifth Avenue.

4. Watrin, J.: Bull. Soc. franç. de dermat. et syph. **31**:41, 1924.

Minor Notes

PAINFUL LINGUAL PAPILLAE

Moses Scholtz, M.D., Los Angeles

I wish to call attention to a minor clinical disorder of the lingual mucous membrane which has been called to my attention on many occasions but of which I have found no mention in the dermatologic manuals.

The patients, mostly middle-aged, wear dental plates and complain of persistently painful spots on the lateral aspects of the tongue near the base. On examination, one sees lesions which are seemingly enlarged or hypertrophied vallate papillae but which show no inflammatory reaction. Repeated electrodesiccation, with or without local anesthesia, reduces the size of the papillae and gives relief from the pain and discomfort.

Two possible explanations for this condition may be considered: first, the possibility of irritation by the dentures and subsequent hypertrophy of the papillae; second, the psychogenic factor of cancerophobia inducing subjective paresthesia. Difference in size between the affected and the normal papillae cannot always be demonstrated objectively, and since minor differences in size are possible in a normal person, this criterion is not of great clinical value.

The clinical point of observation is: Persistently painful spots on the lateral aspects of the tongue (usually vallate papillae) can be relieved by fractional electrodesiccation.

LOTIO ALBA
(Historical Query)

Herman Goodman, M.D., New York

My attention has been recalled to the fact that lotio alba is apparently a prescription of recent origin. It has been used so commonly by dermatologists of the present generation that the impression is probably current that it is one of the ancient prescriptions. Apparently it is not. The first reference to it that I can find is in a footnote to Isador Neumann's "Handbook of Skin Diseases," which was translated by L. D. Bulkley in 1872. On page 202, the translator gives the prescription as having been written by his father, H. D. Bulkley, under the date of May 24, 1870.

Is the introduction of this familar lotion really as recent as that?

INDIFFERENT ELECTRODE IN BIPOLAR DIATHERMY

Ruben Nomland, M.D., Chicago

For the application of this type of diathermy, have the patient lie on a piece of diathermy metal 12 by 30 inches (30.5 by 76.2 cm.) connected to the indifferent terminal of the diathermy machine. The advantages of the method are: No disrobing is necessary, there is no necessity to bandage an inactive electrode on the patient, it is not necessary to have the active cooperation of the patient, and there will be no sparking or discomfort from a poorly applied indifferent electrode.

News and Comment

PROGRAM NOTICE, KANSAS CITY MEETING OF AMERICAN MEDICAL ASSOCIATION, MAY 11-15, 1936

Applicants for a place on the program of the Section on Dermatology and Syphilology of the American Medical Association at the meeting in Kansas City, Mo., from May 11 to 15, 1936, are requested to submit titles and provisional abstracts of their proposed papers to the secretary of the section, Dr. Bedford Shelmire, Medical Arts Building, Dallas, Texas.

Applicants need not be members of this section but must be Fellows of the Association, graduates in medicine not in private practice or invited guests.

AMERICAN BOARD OF DERMATOLOGY AND SYPHILOLOGY

At the meeting of the American Board of Dermatology and Syphilology held in New York on June 9, 10 and 11, 1935, new minimum requirements for admission to the examination of the Board were adopted after the model recently approved by the Advisory Board for Medical Specialties and the Council on Medical Education and Hospitals of the American Medical Association. The Founders Group was abolished, and future applicants will be required to pass the regular examination.

The Board considered 123 applications at this meeting. Sixty-three were certified in the Founders Group, and 42 were certified by examination. The total number of diplomates is now 307. Fifty-two applicants were examined. Of these, 39 passed the examination, and 3 who were reexamined also passed. Five applicants failed, and 5 were conditioned.

Abstracts from Current Literature

EDITED BY DR. HERBERT RATTNER

DERMATITIS GANGRENOSA: A COMPLICATION OF DIABETES MELLITUS. S. S. RIVEN, Am. J. M. Sc. **189**:550 (April) 1935.

In the patient whose case is the subject of this report, the presence of diabetes had been known for three years. Bullous lesions followed by necrosis developed on the back and posterior surface of the thighs and legs. No evidence of atherosclerosis was found. Several explanations are offered for the development of gangrenous lesions in this patient: a vascular disturbance of obliterating type with lesions occurring at points subjected to pressure, slow circulation, an extensive capillary bed, hyperglycemia and bacterial invasion of the skin. The patient recovered in about four months.

ELECTROCARDIOGRAPHIC CHANGES FOLLOWING THE ADMINISTRATION OF POTASSIUM IODID IN SYPHILITIC HEART DISEASE. J. M. BAMBER, Am. J. M. Sc. **189**:681 (May) 1935.

Electrocardiograms of the patient whose case is reported showed certain changes which followed the administration of potassium iodide and occurred only after the administration of that drug. The changes mentioned were variations in the T wave and did not occur during mercurial treatment without iodides. The changes seen in the curves were believed to be due to the effect of the potassium iodide on the syphilitic lesion near the orifices of the coronary arteries.

Bamber believes that further study will cause a change in the ideas regarding the treatment of syphilitic disease of the heart.

JAMIESON, Detroit.

CLINICAL SYPHILITIC NEPHROPATHIES. G. HERRMANN and W. L. WARR, Am. J. Syph. & Neurol. **19**:1 (Jan.) 1935.

Syphilitic involvements of the kidneys, though uncommon, do occur. In each case an outline of the data, such as clinical history and results of physical examination and laboratory studies, that are important in making a diagnosis is set forth. Syphilitic nephropathies are classified into two groups: Group 1 comprises the common clinical types, and group 2, the rare clinicopathologic types.

Instances of transient albuminuria and the acute, subacute and chronic nephrotic syndromes constitute the large proportion of the reported clinical cases. Slight albuminuria is the most common occurrence suggestive of renal damage in syphilitic patients and may be present during the roseolar, or secondary, stage. It is probably a benign type of acute nephrosis. Early acute syphilitic nephrosis appears in the secondary stage, and late acute syphilitic nephrosis is an accompaniment of the tertiary stage. Both are characterized by edema, massive albuminuria, cylindruria and the presence of few, if any, red blood cells in the urinary sediment. There is no retention of nitrogenous waste products, little if any change in the excretion of dye, and no rise in blood pressure. The designation subacute syphilitic nephrosis is applied when the symptoms and signs are found in latent syphilis. Chronic syphilitic nephrosis includes cases with a long history of edema, no rise in blood pressure, persistent albuminuria and slight cylindruria with few if any red blood cells in the sediment and a consistently low protein content of the blood serum.

Three new cases are reported, and a survey of the literature and remarks on therapy are given. It is believed that after a careful study almost any type of antisyphilitic regimen, if begun cautiously with half dosage, is likely to be successful.

REUTER, Milwaukee.

ALLERGY: A REVIEW OF CURRENT LITERATURE. F. M. RACKEMANN, Arch. Int. Med. **55**:141 (Jan.) 1935.

Rackemann reviews recent articles only. In a review of this subject many conditions are touched on which are not of dermatologic interest.

After mentioning the history of allergy Rackemann notes the broadening concept of allergy, such as allergic reactions in connection with trichinosis, hookworm disease, Echinococcus disease, undulant fever, lymphogranuloma inguinale and skin diseases, particularly the group of "dermatids."

In discussing the relation between the various phases of allergy he refers to an article in which he suggested that certain chronic infections represent an early stage of the process of immunity, while asthma, hay fever and eczema represent a later stage, one of the latter conditions remaining because the patient does not escape into the final stage of immunity.

As yet no clinical picture analogous to that of natural hay fever or asthma has been observed, even though it may be easy to produce sensitivity of the skin with the appearance of reagins in the blood.

Studies in the physiology of the blood and endocrine glands have, so far, yielded no knowledge showing a difference between allergic and normal persons. Likewise it has been impossible to show any particular difference in the immunologic responses of normal persons and asthmatic patients.

Woringer divided a group of infants with eczema into two divisions. The patients in one division (*holoallergique*) had antibodies in their blood and reacted with urticarial wheals when tested with egg white; those in the other division (*dermoallergique*) had no demonstrable antibodies in the blood and the sensitivity was present in the skin only. Various writers have recorded cases of asthmatic sensitivity acquired by inhalation of foreign dusts, cases of that type occurring in weavers, workers in clothing warehouses, farmers, bakers, handlers of animals, dyers, seamstresses and nurses. Food has also been incriminated as a sensitizing agent.

In cases of contact eczema the sensitiveness is in the skin only, and if local areas become sensitive to drugs that sensitivity remains in the area in which it originated, even when the skin covering that area is transplanted to normal sites. The results of Wise and Sulzberger differed from those referred to in the foregoing statement, as the reaction did not follow the transplant of sensitive skin but remained in the old sensitive area.

It was found by Simon and Rackemann that guinea-pigs could not be made to show cutaneous sensitivity to Rhus toxicodendron by any method except contact with the skin. Others, however, were able to sensitize skins to foreign proteins by repeated intradermal injections.

Stevens found that of forty-five patients wtih asthma eleven gave negative reactions to cutaneous tests and inhalation tests. Other tests reported by Stevens show that a marked discrepancy exists between the results to cutaneous and those to inhalant tests.

In discussing Kahn's work, "Studies in Tissue Reactions in Immunity," an interesting observation is made regarding spirochetal infection. According to Kahn, the spirochetes meet no resistance until they reach the blood stream. The skin is sensitized in the meantime, but it becomes suddenly desensitized by the circulating antigen, and a necrotic reaction follows.

The work of a number of other investigators is reviewed, but space does not permit the mention of all.

In the diagnosis of asthma, hay fever and eczema, the scratch and intradermal tests were used, the scratch test being satisfactory in 91 per cent of children with hay fever, while in studying patients with asthma it was necessary to use both tests to obtain 87 per cent of positive results.

Two discrepancies in the use of skin tests are pointed out: (1) that skin tests may be positive and yet have no clinical significance and (2) that skin tests may be negative and yet the patient may be sensitive.

The patch test is regarded as a great practical advance in the clinical study of allergy. It is of greatest value in the diagnosis of contact dermatitis.

In the diagnosis of food allergy, Vaughan's method is to check the total number of leukocytes. It was found that after the patient had eaten certain foods to which he was sensitive the number of leukocytes fell, the degree of fall and degree of clinical sensitivity being proportional.

The greatest emphasis is given to the taking of the clinical history. This, says Rackemann, should be taken by a detective rather than by a physician and should go into minute and exact details of every phase of the patient's life, food, occupation, etc. If the history is taken accurately enough, sensitization tests will be almost unnecessary.

Mention is made of the work on drug allergy in connection with certain drugs in the production of agranulocytosis and of the question of thrombo-angiitis obliterans being due in part to sensitivity to tobacco.

Vaughan has given figures showing that 10 per cent of the population have a major allergy and 50 per cent have allergy as a minor manifestation.

Migraine, epilepsy, gastro-intestinal allergy, cold allergy, the Arthus phenomenon and anaphylactic shock are briefly discussed.

The review concludes with a discussion as to the treatment of hay fever, studies on asthma and a bibliography of articles mentioning new articles on the cause of allergy.

PERSISTENT ABNORMALITIES (WASSERMANN FASTNESS) OF THE SPINAL FLUID IN TREATED NEUROSYPHILIS: THEIR PROGNOSTIC IMPORT. M. J. GOODMAN and J. E. MOORE, Arch. Int. Med. **55**:826 (May) 1935.

In the selection of 212 cases for study, only those were included in which prolonged treatment had resulted in symptomatic improvement or complete relief and those in which neurologic and serologic examinations had been continued for at least two years after cessation of treatment.

In 95 patients the spinal fluid showed a persistently positive Wassermann reaction; in 117 patients the reaction was reversed by treatment. In the group with the persistently positive reactions 21 patients showed progression of symptoms; most of these progressions occurred in patients observed for from two to five years after treatment. In the other group only 8 patients showed progression, and in these, likewise, the clinical progression appeared in the earlier years of observation. In both groups the lower percentage of clinical progression was noted in patients who had been treated for over two years. A contrast was noted in the two groups according to the type of involvement, parenchymatous and nonparenchymatous. The incidence of progression of parenchymatous neurosyphilis was 33.3 per cent in the Wassermann-fast group and 19.3 per cent in the group with reversed reaction. In the patients with nonparenchymatous syphilis relapse was quite frequent, but the total incidence of progression was surprisingly low. In this last group, however, subsequent relapse was often of the dementia paralytica type. Thirty-one of the patients had received fever therapy at some time, and subsequent progression was noted in only two of these.

While it is believed that the reaction of the spinal fluid and the clinical outcome in cases of neurosyphilis bear a definite relationship, it is not inevitable that progression must occur in patients with a persistently positive reaction. Likewise, the rate of reversal of the reaction cannot be used as a guide to the amount or duration of treatment to be administered in cases of neurosyphilis.

JAMIESON, Detroit.

ERYTHEMA NODOSUM AND FOCAL INFECTION. L. BEDFORD ELWELL, Brit. M. J. **1**:974 (May 11) 1935.

A case is reported of recurrent erythema nodosum in a nurse, aged 29. The attacks were induced by an axillary lymphadenitis, and the maximum intensity of

the eruption was concomitant with suppuration of the axillary glands. Evacuation of the pus was followed by immediate relief from the attack of erythema nodosum, but the relief was not permanent until every focus of dental sepsis had been eradicated. It seemed certain that neither Mycobacterium tuberculosis nor Streptococcus haemolyticus was a factor in this case. The article contains a concise review of the literature dealing with the etiology of erythema nodosum.

A Treatment for Warts. Stuart McAnsland, Brit. M. J. **1**:1123 (June 1) 1935.

Two cases are reported in which cure was obtained by the continuous application of elastoplast (zinc oxide spread on an emulsion of gelatin and rubber and incorporated with a cotton elastic bandage).

Wood's Light and Ringworm of the Scalp. F. A. E. Silcock, Brit. M. J. **1**:1239 (June 15) 1935.

In a brief communication, Silcock reports on some experiments which tend to show that "all that fluoresces is not fungus." Various colors were obtained with petrolatum, liquid petrolatum, quinine hydrochloride and quinine sulphate in solution, etc. Fluorescence of the scalp should not be considered as indicating ringworm before the scalp has been cleansed thoroughly with green soap to remove grease and scales.

Rattner, Chicago.

The Skin Conditions Found in Loa Loa Infections. G. C. Low, J. Trop. Med. **37**:359 (Dec. 1) 1934.

In connection with the infestation by the parasite *Loa loa* there occur certain swellings of the skin referred to as "Calabar swellings."

These lesions occur in both white persons and Negroes and bear some resemblance to angioneurotic edema, as they are egg-sized, painless and somewhat hot. They usually disappear in a few days. The parasite inhabits the subcutaneous tissues and wanders about freely. It has been suggested that the swellings are due to the toxins arising from a dead parasite.

Pruritis and giant urticaria may also be encountered.

In the diagnosis of infestation with Loa loa one must consider the question of the actual presence of the worm, the presence of embryos in the peripheral blood, the history of Calabar swellings, the eosinophilia with no explainable cause and Fairley's filarial skin test.

Acladiosis and Paracladiosis. A. Castellani and I. Jacono, J. Trop. Med. **37**:360 (Dec. 1) 1934.

Acladiosis is described as a condition in which ulcerative lesions are present chiefly on the skin of the trunk and extremities; the lesions are sharply defined, are roundish or oval and have a base studded with rather prominent red granulations.

The condition is found chiefly in Ceylon, the Malay States, South America and Macedonia and is due to a fungus isolated in Ceylon to which has been given the name Acladium Castellani. In cases of acladiosis the Wassermann reaction of the blood is negative, and the diagnosis can be made with certainty only when the fungus is found.

Potassium iodide in large doses is the most efficient treatment, with local application of antiseptics for cleansing the ulcers. Arsenic and mercury have no effect on the disease.

Lesions due to paracladiosis are rupioid, yellowish and from 2 to 4 cm. in diameter, and they may be present over the whole body. In the case reported the crusts were thick but on removal revealed no true ulcerations but rather a condition resembling psoriasis. Intense pruritus was present as well as lymphadenitis.

The Wassermann test was negative, and the blood showed no changes.

This disease occurs in Central China and is caused by a fungus which Castellani and Jacono identified as Ascothrica chartarum Berkeley, 1838, var. orientalis Castellani and Jacono, 1934.

Castellani's fuchsin paint was found to be the most efficacious agent for treatment.

TINEA IMBRICATA (TOKELAU). A SHORT GENERAL ACCOUNT WITH REPORT OF A CASE IN A EUROPEAN. A. CASTELLANI, J. Trop. Med. **37**:363 (Dec. 1) 1934.

Castellani gives an interesting historical account of tinea imbricata and lists the various synonyms by which it is known and the regions where it is most commonly found, i. e., the Pacific Islands, Southern China, the Malay States, Ceylon and India.

The disease is believed to be due to a group of fungi rather than to a single species, and Castellani gives in detail the cultivation of the fungus, the histopathologic picture of the lesions, etc., and reports a case occurring in a European.

Complete cure is difficult to obtain, as relapses occur as soon as treatment is discontinued. Initial lesions may be easily treated by applications of fuchsin paint or a similar fungicidal preparation.

TINEA DECALVANS PERSTANS. A. CASTELLANI, J. Trop. Med. **37**:368 (Dec. 1) 1934.

Tinea decalvans perstans is described as tinea of the scalp characterized by white patches composed of scales followed by permanent alopecia.

It occurs in Ceylon and China and is due to a fungus designated as Trichophyton violaceum Bodin var. decalvans Castellani.

In the course of the disease the whitened scaly patches and the hair of those areas disappear, leaving smooth bald patches which are permanent.

(Photographs accompanying the article make one think of severe syphilitic alopecia from the "moth-eaten" effect produced. Abstracter.)

KERATOMA PLANTARE SULCATUM (CASTELLANI). C. G. AARS, J. Trop. Med. **37**:372 (Dec. 1) 1934.

This condition was first named and described by Castellani. All the patients observed by Aars were men, natives of Dutch Guiana, and all were accustomed to go barefooted.

The outstanding symptoms consisted of a marked thickening of the horny layer of the soles, the presence of numerous holes of varying sizes and depths and the development of many furrows later. The holes and sulci never extended deeper than to the inner parts of the stratum corneum.

Seasonal changes are believed to be due to the action of mud, water, heat, trauma, etc. The palms of these patients were not involved.

Aars considers the condition a primary hyperkeratosis not due to yaws or to a fungous infection.

JAMIESON, Detroit.

THE USE OF FLUORESCEIN IN LEPRA REACTION. GORDON A. RYRIE, Leprosy Rev. **5**:12 (Jan.) 1934.

The syndrome known as the "lepra reaction" may include a number of different entities which may, in themselves, require varied forms of treatment. The author is not enthusiastic about his results, as he is cognizant of the difficulties in evaluating the efficacy of a new drug. He summarizes his article by saying that in a large proportion of cases fluorescein is more beneficial than mercurochrome, to which it is chemically related. It is less toxic and can be given in larger and more frequent doses. It is more effective when treatment with calcium and milk and the following of a diet with a high vitamin content precede the injections.

The use of the drug is not contraindicated for patients with diseases of the kidneys and it is not detrimental to the patient when the treatment is prolonged.

[An important precautionary measure to be adhered to is the avoidance of exposure to sunlight after injections of fluorescein, as it has been shown experimentally that rabbits are killed when exposed to sunlight after injections of fluorescein. Abstracter.]

CHAULMOOGRA OIL IN THE TREATMENT OF LEPROSY. P. D. STRACHAN, Leprosy Rev. **5**:16 (Jan.) 1934.

The type of case, the number of injections given and the proper observation of controls should receive due consideration before any statistical study evaluating the results of any treatment is made. Treatment alone cannot control leprosy; more emphasis should be placed on the prevention. [The chaulmoogra (hydnocarpus) preparations are not specific for leprosy but have stood the test of time. Abstracter.]

LEPROSY IN INDIA AND CEYLON. R. G. COCHRANE, Leprosy Rev. **5**:28 (Jan.) 1934.

Cochrane comments on resolutions and recommendations passed by the All-India Leprosy Conference and stresses the following points as being important in controlling the disease: 1. Leprosy is a preventable disease. 2. Not all patients with leprosy necessarily need treatment, and this applies to patients with early as well as with late stages of the disease. 3. Treatment cannot bring certain cases to a stage of noninfectivity. 4. Isolation in certain cases is essential. 5. The seriousness of the problem is not uniform; certain areas may need special concentration. 6. Leprosy is only one of the endemic diseases and its control should be a part of a general system for the safeguarding of the public health.

RESULTS OF THE CHAULMOOGRA TREATMENT IN VERY EARLY CASES OF LEPROSY. JOSE RODRIGUEZ, Leprosy Rev. **5**:102 (July) 1934.

Rodriguez reviews a nine year follow-up of cases of leprosy. His study was based primarily on "bacteriologically negative" lesions consisting of macules and localized areas of anesthesia. The efficacy of a treatment should be judged by its ability to arrest the condition so that the lesions do not become infected with the pathogenic organism. In this study, 336 children of leprous parents were treated intensively with iodized ethyl esters and followed for five years. It was concluded that the treatment in the stages designated as "suspicious" "prodromal" and "early clinical" was not effective and that it was of value only when the organisms had appeared in typical form in the lesions.

Results of treatment of neural or macular leprosy with the chaulmoogra preparations are more disappointing in the early stages of anesthetic or macular leprosy before the bacteria have invaded the lesions than in the stages in which the cutaneous lesions show acid-fast bacilli.

The author theorizes and offers a hypothesis to explain the development of the leprotic lesions and the variable paradoxical results of the chaulmoogra preparations: The life history of Mycobacterium leprae is reviewed.

ETHYL ESTERS OF "PONGAMIA GLABRA" IN THE TREATMENT OF LEPROSY. G. R. RAO, Leprosy Rev. **5**:127 (July) 1934.

In the treatment of leprosy, according to the Ayurvedic system, five oils have been recommended. The oil of Hydnocarpus wightiana has been used as the drug of choice, and that of Pongamia glabra is the second choice. The latter drug has been avoided on account of the pain resulting from its administration and the difficulty attendant on its preparation. A technic of preparation is described. In a series of seventeen cases, a sterilized ester was used intradermally. The drug

apparently had no effect on Mycobacterium leprae, as the basis for improvement was on clinical grounds only. An interesting observation is noted with the use of this drug, namely, that it has a melanogenetic or melanopoietic effect on depigmented areas. The degree of hyperpigmentation produced by the drug was directly proportional to the natural complexion of the patient. Three patients with leukoderma were treated with this drug, and a favorable response was noted in two of them.

Examination of Bone Marrow for M. Leprae. H. H. Gass and D. P. Rishi, Leprosy Rev. **5**:144 (July) 1934.

The microscopic examination of the bone marrow of sixty-nine patients with leprosy was studied in the Chandkhuri Leprosy Hospital. Most of the specimens were obtained from necrosed bones which had been removed surgically; some were obtained from autopsy material. Asepsis in obtaining the material was carefully observed. The bone marrow of seventeen of twenty-one patients with mixed (cutaneous and neural) leprosy was positive for Mycobacterium leprae. Three of the four specimens that did not show the organism were from smears taken from the phalanges or from parts of phalanges, and one was from a metatarsal bone. Among specimens from the forty-eight patients whose disease was classified as neural leprosy not a single smear of bone marrow showed acid-fast bacilli.

Baer, Pittsburgh, Pa.

Toxic Encephalitis Following Use of Thallium Acetate. F. Pozzo and M. J. Tarquina, Prensa méd. argent. **21**:374 (Feb. 21) 1934.

A child 7 years old had typical toxic encephalitis. Thallium acetate in normal doses had been used. The spinal fluid was normal, as was the blood. In addition to presenting the symptoms of encephalitis the child lost all her hair, as is usual in cases of thallium poisoning. Pozzo and Tarquina discuss the toxicology of thallium compounds, review the literature and warn against the use of those compounds.

Sanford, Chicago. [Am. J. Dis. Child.]

Etiology of Lupus Erythematosus. Donges, Dermat. Wchnschr. **99**:1369 (Oct. 20) 1934.

Donges discusses briefly the etiologic factors of lupus erythematosus, especially its possible connection with syphilis. His patient, a woman aged 38, had extensive, severe lupus erythematosus which had been present for twelve years. She also had a positive Wassermann reaction of the blood. She was given neoarsphenamine, bismuth compound and a gold preparation. The eruption cleared entirely. Three possibilities must be considered: (1) the coincidental presence of lupus erythematosus and latent syphilis; (2) the existence of lupus erythematosus on a syphilitic ground, perhaps with a syphilitic endocrine malfunction; (3) the absence of syphilis but the presence of lupus erythematosus with a nonspecific Wassermann reaction. These possibilities are briefly considered, but no definite conclusion is reached.

Lichen Planus of the Mucous Membrane of the Mouth Following Therapeutic Use of a Gold Preparation. B. H. U. Mohrmann, Dermat. Wchnschr. **99**:1373 (Oct. 20) 1934.

A 40 year old man was given a course of treatment with a gold preparation in an attempt to reduce a persistently positive Wassermann reaction. A stomatitis suggestive in appearance of lichen planus developed on the mucous membrane of the mouth. This stomatitis was not affected by intravenous administration of sodium thiosulphate but cleared under therapy with an arsphenamine preparation.

Importance of the Influence of Mineral Salts on the Pathogenesis of Cutaneous Tuberculosis. E. Keining and G. Hopf, Dermat. Wchnschr. **99**:1397 (Oct. 27) 1934.

A salt-poor diet is ineffective in the treatment of pulmonary tuberculosis though it is helpful in that of cutaneous tuberculosis as well as in that of other conditions, such as urticaria, eczema and Duhring's disease. This is due to the effect of the sodium portion on the neurovegetative system, and the result of its withdrawal is thus indirect rather than direct.

Unusual Eruption Resembling Parasitic Eczema and Healing with Pigmentation Developing in the Course of Treatment of Syphilis Complicated by Hypernephroma. Walter Blume, Dermat. Wchnschr. **99**:1406 (Oct. 27) 1934.

Blume describes the case of a 45 year old patient in whom a circinate scaly eruption of the trunk and limbs developed during a course of treatment with arsphenamine and a preparation of mercury. This became diffuse and then cleared, leaving a diffuse brown pigmentation. An abdominal tumor developed which led to the patient's death. Necropsy showed the presence of a hypernephroma. Blume discusses the question of the cause of the pigmentation. Either the arsphenamine (neosilver arsphenamine) or the adrenal tumor could be responsible.

A Case of Psoriasis Arthropathica (?). Ernst Rodner, Dermat. Wchnschr. **99**:1438 (Nov. 3) 1934.

A typical case of psoriasis arthropathica is described. The patient was a man aged 32. Psoriasis had been present for twelve years, and arthritis had existed for six years. There was no history of psoriasis or of arthritis having occurred in the family. The arthritis was of the destructive type. Exacerbations of psoriasis and arthritis did not occur simultaneously.

The Question of Pseudosyphilis Papulosa. H. Höcker, Dermat. Wchnschr. **99**:1469 (Nov. 10) 1934.

Lipschütz described the syndrome of pseudosyphilis papulosa in 1921. Since then only twelve cases have been recorded, all of which occurred in females. The condition consists essentially in the eruption of from one to several grouped papules ranging in size from that of a pinhead to that of a lentil. There are no subjective symptoms, and the lesions are located on the labia or around the anus. There is no inflammatory reaction. As a rule the papules clear when the patient is hospitalized for a short time and receives indifferent treatment. Cleanliness is apparently of importance. All signs of syphilis are absent. Höcker adds to the literature reports of two new cases, one occurring in a man, and describes the histologic picture which consists chiefly of acanthosis with cellular and intercellular edema. There is a moderate infiltration of lymphocytes in the upper portion of the dermis. The vessels are somewhat dilated, and their number is increased.

Hypersensitivity to Vanilla. G. E. Sincke, Dermat. Wchnschr. **99**:1480 (Nov. 10) 1934.

Sincke reports the case of a patient with a dermatitis due to vanilla. Intracutaneous tests showed that she was not sensitive to chemically pure vanilla but only to the commercial product.

A Case of Arterial Angiomyoneuroma (Masson). Toshio Aisu, Dermat. Wchnschr. **99**:1532 (Nov. 24) 1934.

In a man aged 37 a painful nodule developed on the volar surface of the left thumb. When the lesion was excised it proved to be a circumscribed elastic mass with a rather definite capsule exhibiting the histologic picture of an angiomyoneuroma.

FORMATION OF STONES IN THE LEFT NERVUS AURICULARIS MAGNUS ASSOCIATED WITH AN ANESTHETIC ZONE IN THE FOSSA RETROMANDIBULARIS. M. OTA and S. SATO, Dermat. Wchnschr. **99**:1590 (Dec. 8) 1934.

In a 25 year old farmer who had had an anesthetic zone in the left fossa retromandibularis the great auricular nerve presented a hard tumor 3.5 cm. long. Histologically there was thickening of the epineurium, which contained a structureless calcified mass. Whether this calcification was tuberculous, leprous or due to neither tuberculosis nor leprosy could not be determined.

THE PROPHYLACTIC EFFECT OF ULTRAVIOLET RAYS ON DERMATITIS DUE TO CHRYSAROBIN IN PSORIASIS VULGARIS. L. N. MASCHKILLEISSON and L. A. ABRAMOWITSCH, Dermat. Wchnschr. **99**:1614 (Dec. 15) 1934.

Preliminary ultraviolet irradiation does not prevent dermatitis due to chrysarobin, but it does increase the therapeutic effect of the drug.

CUTANEOUS MILIA. FRIEDRICH DIETEL, Dermat. Wchnschr. **99**:1637 (Dec. 22) 1934.

A case of secondary milia is described. They developed in groups on the backs of the hands after a dyshidrotic eczema. Histologic examination showed that they were closely related to the sweat ducts.

INDUSTRIAL STIGMA OF SEAMSTRESSES. W. ENGELHARDT, Dermat. Wchnschr. **99**:1640 (Dec. 22) 1934.

In two seamstresses keratotic lesions developed on the elbows. The lesions were of long duration and were undoubtedly caused by the rubbing of the elbows on the table of the sewing machine. The condition is to be considered as an industrial stigma.

MAY OCCIPITAL PUNCTURE BE USED IN THE CONSULTING ROOM? HANS J. SCHMITZ, Dermat. Wchnschr. **99**:1648 (Dec. 22) 1934.

Schmitz has performed several hundred occipital punctures on ambulatory patients with only one accident, which was not fatal. He stresses the importance of a careful technic and the necessity of preliminary training.

THE ETIOLOGY AND CLINICAL FEATURES OF ACANTHOSIS NIGRICANS. ERWIN BODENSTEIN, Dermat. Wchnschr. **99**:1670 (Dec. 29) 1934.

A typical case of acanthosis nigricans is described. The patient was a woman aged 38 who also had an extensive abdominal carcinoma. Functional tests of the glands of internal secretion by means of the interferometric method of Abderhalden indicated a marked variation from the normal in the function of the adrenal glands. Bodenstein suggests that the cutaneous disorder in these cases may be linked with a disturbance of the function of the endocrine glands.

PRINCIPLE AND PERFORMANCE OF THE SPECIFICALLY SENSITIZED WASSERMANN TEST. H. T. SCHREUS, Dermat. Ztschr. **70**:121 (Nov.) 1934.

Schreus refers to previous communications (*Ztschr. f. Immunitätsforsch. u. exper. Therap.* **82**:53 and 59 [March 15] 1934) in which in collaboration with Foerster he described a method of increasing the sensitivity of the Wassermann reaction without unduly increasing the percentage of nonspecific reactions. He presents a table showing the results on 631 serums and comparing the percentages of positive reactions to the Wassermann test, the Schreus sensitized Wassermann test and the precipitation test. The sensitized reaction stands between the standard Wassermann and the precipitation test as to sensitivity but produced only 0.3 per cent of nonspecific reactions as compared to 1.5 per cent, the figure for the precipitation test.

THE HISTOLOGIC FINDINGS IN ARGYRIA CUTIS. J. J. ZOON, Dermat. Ztschr. **70**:125 (Nov.) 1934.

Frozen sections were made of material taken from two patients, one with generalized and the other with localized argyria. They were stained with hematoxylin and eosin, orcein and hematoxylin and polychrome blue and examined both by direct illumination and by means of the dark field. The dark field made visible particles which could not be seen under direct illumination. The results of the examination in the two cases were the same. No silver was seen in the epidermis. It had a special affinity for: (1) a subepidermal connective tissue border, (2) the elastic fibers, (3) the membrane of connective tissue around the sweat and sebaceous glands and the hyaline membrane of the follicles, (4) the walls of the vessels and (5) the collagenous tissue.

In addition, small amounts of the metal could be observed in the connective tissue cells, in the endothelial cells of the vessels and in the many mast cells present.

INOCULATION OF PARALYTIC PATIENTS WITH FRAMBESIA. P. J. VAN DER SCHAAR, Dermat. Ztschr. **70**:185 (Dec.) 1934.

Forty-one patients with syphilis of the central nervous system were inoculated with material containing Spirochaeta pertenuis from seven different patients with yaws. In most instances serum was applied to a scarified area, but in some transplantation of tissue was the method used. A positive reaction occurred in one patient, and he had a negative Wassermann reaction of the blood and spinal fluid. Van der Schaar concludes that the relationship between S. pertenuis and Spirochaeta pallida is so close as to cause an immunity for both. He admits that an asymptomatic infection is possible but regards it as unlikely. His work indicates that vaccination with yaws cannot be expected to be of therapeutic benefit in syphilis of the central nervous system.

THE SOURCE OF THE PORPHYRIN FLUORESCENCE IN THE MOUTH AND ON THE SKIN. C. CARRIÉ, Dermat. Ztschr. **70**:189 (Dec.) 1934.

It is known that ultraviolet rays filtered through a Wood glass and a solution of copper sulphate cause a red fluorescence of the follicular openings, tongue and teeth and scales of psoriasis. This phenomenon is due to the presence of coproporphyrin. In order to determine the source of this substance, Carrié cultured material from the teeth and tongue on Sabouraud's medium and obtained various pure cultures. These were transplanted to a special medium (Fink's) consisting of: water, 1,000 parts; saccharose, 100 parts; urea, 1 part; calcium chloride, 0.5 parts; magnesium sulphate, 0.4 parts; monopotassium phosphate, 0.75 parts, and disodium phosphate, 0.25 parts. After from eight to fourteen days the culture showed a red fluorescence under the Wood filter. The organism responsible was found to be a gram-positive bacillus which was nonhemolytic, grew best on ordinary agar at 37 C. and was a saprophyte on normal skin and mucosa. This work indicates that the coproporphyrin is not due to a breaking down of blood pigment as was previously believed.

INFLUENCE OF THE AMOUNT OF CULTURE MEDIUM, "LIGHT" AND QUANTITY OF INOCULATED MATERIAL ON THE GROWTH OF FUNGI. H. HRUSZEK, Dermat. Ztschr. **70**:197 (Dec.) 1934.

Hruszek shows by a series of experiments that the growth of fungi is practically unaffected when the cultures are subjected to roentgen irradiation or enclosed in cellophane bags of various colors. The amount of material transferred has a direct bearing on the rate of development of the colony: The greater the concentration of the fungus planted, the more rapid the growth of the colony. Likewise, in small cultures the growth is more rapid in deep than in shallow culture mediums.

CHEILITIS EXFOLIATIVA ET GLANDULARIS. A. IORDAN and A. TARABUCHIN, Dermat. Ztschr. **70**:249 (Jan.) 1935.

Fourteen cases of exfoliative cheilitis and four of glandular cheilitis are briefly described. Iordan and Tarabuchin conclude that: 1. The exfoliative form is more common than the glandular. 2. Both occur more commonly in men. 3. External irritation plays a part in the etiology. 4. The glandular form is more frequently seen in younger persons. 5. Cheilitis glandularis appears in three forms, cheilitis glandularis simplex of Puente and Acevedo, Baelz's disease and Volkmann's cheilitis glandularis apostematosa. These forms of the disease vary in degree only. 6. Treatment of both types of cheilitis is unsatisfactory. The best results followed the local and internal use of aqueous solution of iodine and irradiation. 7. The prognosis is doubtful, as malignant degeneration may occur in either form of cheilitis.

COMPLEMENT FIXATION IN FUNGOUS DISEASES. F. FÖLDVÁRI, Dermat. Ztschr. **70**:260 (Jan.) 1935.

Földvári was able to demonstrate the presence of complement-fixing antibodies in all cases of deep trichophytosis and in some cases of superficial dermatomycosis. In some instances vaccine therapy increased the reaction; in others it did not change it. There was no evidence that the variation of the titer of the antibodies bore any relation to the prognosis.

EXANTHEMS IN SEPSIS WITH SPECIAL REFERENCE TO THAT CAUSED BY PNEUMOCOCCI OR BY COLON BACILLI. VIKTOR WILLARD, Dermat. Ztschr. **70**:271 (Jan.) 1935.

Willard discusses the cutaneous manifestations which occur in the various types of septicemia. He points out that eruptions are relatively common in cases of staphylococcic and streptococcic septicemias but are rare in cases of infection of the blood due to colon bacilli or to pneumococci. Frequently the eruption occurs shortly before death. One fatal case of septicemia due to colon bacilli is described in which the pustular character of the eruption suggested the probability of an embolic origin. Willard describes two of his own cases of pneumococcic septicemia. One of the patients had an erythematous eruption with small pustules in which the pneumococcus was demonstrated. The other presented a roseola-like eruption and died. From the statistics it is concluded that exanthems occur in about 5 per cent of the cases of pneumococcic septicemia. The mechanism may be toxic or embolic.

MULTIPLE FIBROMATOSIS OF THE SKIN DUE TO FROST-BITE. D. A. ZIPERSSON, Dermat. Ztschr. **70**:279 (Jan.) 1935.

A 30 year old woman had been exposed to severe cold when she was 2 years old. After this exposure the skin of the face and back was reddened, and numerous nodules varying in size from that of a pinhead to that of a bean and larger developed. The tumors were particularly numerous on the face and back. The mucous membrane of the lip and mouth was involved. The scalp, the anterior surface of the neck and the extremities were the only uninvolved areas. Histologic examination of several of the tumors confirmed the diagnosis of fibroma. The condition is to be differentiated from the lenticular dermatofibromas (Schreus) or the cutaneous nodules first described by Arning and Lewandowsky in 1911.

A REVIEW OF THE TWENTY-FIVE YEAR PERIOD SINCE THE INTRODUCTION OF EHRLICH'S ARSPHENAMINE IN THE TREATMENT OF SYPHILIS. ERICH HOFFMANN, Dermat. Ztschr. **70**:309 (Feb.) 1935.

Hoffmann recalls the history of the introduction of arsphenamine and reviews a number of the cases that occurred in the early part of the period in which

relatively little treatment resulted in a permanent cure. He stresses the fact that with the development of modern methods of combined treatment the disease has become readily controllable and curable in a high percentage of instances.

CAN A POSITIVE SERUM REACTION IN SYPHILIS BECOME NEGATIVE WITHOUT TREATMENT? H. BOAS, Dermat. Ztschr. **70**:318 (Feb.) 1935.

Boas reports the case of a woman who gave birth to a macerated fetus. At that time and for two months after delivery the blood serum gave a positive reaction to the Wassermann, Kahn, Meinicke and Müller tests. About three months after the delivery the patient had a mild febrile (temperature 38 C. [100.4 F.]) parametritis. After this all the tests were negative. There was no history of syphilis. [It is to be noted that none of the reactions was strongly positive. L. T.]

THE INFLUENCE OF THE WAR AND POSTWAR PERIODS ON PSORIASIS AND CUTANEOUS TUBERCULOSIS. W. ENGELHARDT and W. CORDES, Dermat. Ztschr. **70**:321 (Feb.) 1935.

It is shown that during the World War the incidence of psoriasis decreased while that of cutaneous tuberculosis increased. With the resumption of normal conditions the opposite became true. This phenomenon is probably due to the diet poor in meat and fat which is consumed in hard times. The authors conclude that the evidence adduced is additional proof for the conception of psoriasis as a hereditary disease due to a disturbance of fat metabolism.

FUNGUS CULTURES ON SLICES OF CUCUMBER: A NEW NATURAL CULTURE MEDIUM FOR PRIMARY AND PASSAGE CULTURES. H. HRUSZEK, Dermat. Ztschr. **70**:341 (Feb.) 1935.

Slices of cucumber were found to be a suitable culture medium for several fungi. The characteristic growths were well shown. The technic of the preparation of this medium is described.

THE RELATIONSHIP BETWEEN THE VIRUS OF ZOSTER AND THAT OF VARICELLA. J. M. LEWIN, Dermat. Ztschr. **70**:346 (Feb.) 1935.

Lewin describes a case in which bilateral zona occurred on the upper extremities. A week after the zoster cleared typical varicella developed. The author concludes that this is proof that the virus of zoster and that of varicella are frequently not identical.

THE INFECTIVITY OF VARIOUS ANIMALS, ESPECIALLY OF VARIOUS TYPES OF MICE, TO SYPHILIS. FRANZ JAHNEL and BERTA SCHARBER, Dermat. Ztschr. **71**:1 (March) 1935.

Jahnel and Scharber report the results of inoculations of syphilis in a variety of animals, particularly various types of mice. Consideration is given to the manner of living of these animals.

DOES A POSITIVE WASSERMANN REACTION OCCUR OCCASIONALLY IN FEBRILE PULMONARY CONDITIONS? HARALD BOAS and I. C. NEERGAARD, Dermat. Ztschr. **71**:6 (March) 1935.

With the technic employed at the State Serum Institute in Copenhagen a positive Wassermann reaction occurred in 0.33 per cent of patients with febrile pulmonary conditions. However, it is necessary to perform the test with special care in the presence of febrile disorders.

TAUSSIG, San Francisco.

Society Transactions

PHILADELPHIA DERMATOLOGICAL SOCIETY

VAUGHN C. GARNER, M.D., *Secretary*

April 26, 1935

ROBERT L. GILMAN, M.D., *Chairman*

ACROCYANOSIS. ENDOCRINOPATHY. Presented by DR. S. S. GREENBAUM.

A. K., a woman aged 47, shows reticulated and diffuse violaceous erythema involving both breasts, the lower extremities and, to a less extent, the upper extremities; there are two large keloids over the sternum and back. The patient relates the appearance of the condition to a period following the birth of her last child, fifteen years ago. She has otherwise enjoyed good health all her life. From 1925 to 1933 her weight increased from 165 to 255 pounds (74.9 to 115.7 Kg.). At present, after dieting, she weighs 215 pounds (97.6 Kg.). Laboratory tests gave the following results: On Feb. 22, 1935, the basal metabolic rate was plus 22; on April 23 it was plus 26. The test for dextrose tolerance made on April 9 gave the following values for sugar: blood, 131 mg. per hundred cubic centimeters, and urine, 0; blood, 166 mg., and urine, 0; blood, 234 mg., and urine, 0.24 per cent. The blood count was normal.

DISCUSSION

DR. S. S. GREENBAUM: The patient is presented because of the fact that in some cases of acrocyanosis definite endocrine disturbances are found. She showed a low tolerance for dextrose and a high metabolic rate on two occasions. I believe that all cases of acrocyanosis should be studied from the standpoint of endocrinopathy. The keloids presented by this patient are apparently incidental.

ACRODERMATITIS CHRONICA ATROPHICANS. Presented by DR. B. L. KAHN for DR. S. S. GREENBAUM.

F. R., a woman aged 60, presents a symmetrical eruption on both upper and lower extremities; there are marked atrophy of the skin and dilated capillaries. The patient has keratotic lesions on both hands. She was first seen in 1922, at which time she had dry erythematous lesions on both legs and marked varicosities. The skin was atrophic and shiny, and the ankles were edematous. In 1934 she returned with atrophy of all layers of the skin on parts distal to the middle portion of the thighs and on both forearms. A similar condition existed on the forehead, face and upper part of the neck and chest. Laboratory tests showed that the urine was practically normal except for a faint trace of albumin and occasional hyaline casts. The blood count was practically normal; chemical examination of the blood showed: urea, 30 mg. per hundred cubic centimeters; urea nitrogen, 14 mg., and sugar, 110 mg.

DISCUSSION

DR. THOMAS BUTTERWORTH, Reading, Pa.: This case is interesting because the patient has two infiltrated bands extending down the ulnar surface of both forearms; half-way to the wrist these bands are fixed to the skin. About the knees there are several of the subcutaneous nodules the occurrence of which is described in connection with this disease.

TINEA? PUSTULAR PSORIASIS? DERMATITIS REPENS? Presented by DR. CARROLL S. WRIGHT.

In A. B., a girl aged 12, there developed eight months ago a yellowish discoloration, dryness and loss of the nail of the third finger of the left hand. Trophic

changes subsequently developed in the nails of the first and fourth fingers and in the nails of both big toes. A dry, scaly, slightly itching eruption then appeared on the left heel; its appearance was followed by that of similar patches on both big toes, the ball of the left foot and the extensor surfaces of both legs. On the legs the patches were definitely follicular. There was no previous history of psoriasis or dermatophytosis. Repeated examinations of scrapings from the nails and of material from the cutaneous lesions did not show fungi.

DISCUSSION

DR. F. D. WEIDMAN: I think that this is a fungous infection. The main argument against this diagnosis is the lack of success in demonstrating the fungus. The one thing that influences me more than anything else in suggesting this diagnosis is a circumscribed patch on the shin in which there are definite follicular lesions. That lesion is a perfectly classic lichen trichophyticus of Jadassohn, and I suggest that further search for the fungus be instituted in material from that patch. In collecting the scrapings one should press down firmly enough to get out some of the lanugo hairs by the roots, and these hairs should be examined for evidence of the fungus.

DR. H. J. SMITH: The patient has lesions on both legs that I think are quite typical of psoriasis. The lesions on the feet and fingers do not look at all like psoriasis, but I thought that they might be lesions of the pustular type.

LUPUS ERYTHEMATOSUS AND EFFECTS OF ORAL ADMINISTRATION OF A GOLD PREPARATION. Presented by DR. B. L. KAHN for DR. S. S. GREENBAUM.

R. Z., a girl aged 10½ years, presents erythematous, slightly scaly patches of one year's duration and a few papules on both cheeks. The tuberculin test was negative. Urinalysis gave practically normal results except for a faint trace of albumin. Chemical examination of the blood showed: sugar, 91 mg. per hundred cubic centimeters; urea nitrogen, 11 mg.; chlorides, 545 mg. The treatment has consisted of administration of 0.001 mg. of gold sodium chloride, 0.325 Gm of quinine sulphate three times daily by mouth. The lesions cleared completely under this medication and reappeared when the medication was stopped.

DISCUSSION

DR. S. S. GREENBAUM: The patient is presented because of the excellent results which followed the oral administration of the gold salt. The eruption, as now seen, is a relapse following discontinuance of treatment. When the patient first came to the clinic the eruption was about half as extensive as it is tonight; it disappeared completely under therapy. Then the treatment was deliberately discontinued, and within a week or ten days there was a gradual reappearance of the condition, which is now worse than when the patient was first seen.

NOTE: Gold sodium chloride was subsequently administered by mouth, and rapid improvement occurred.

BILATERAL TUBERCULOSIS OF THE AXILLAE (TUBERCULOSIS COLLIQUATIVA?). Presented by DR. ALLEN D. KING.

E. E., a girl aged 15, has three chronic inflammatory nodules in each axilla; these lesions break down, form chronic draining sinuses and eventually heal with cicatricial scars. There has never been any massive axillary adenopathy. The condition is resistant to all therapeutic measures. The typical lesion is a coin-sized, bluish-red, granulating nodule which appears to involve the deeper layers of the skin but not the lymph nodes or the deeper structures. A purulent exudate covers each inflammatory area, and pressure causes a small quantity of pus to exude from the depths. There are no apple jelly nodules. A smear from the exudate showed numerous acid-fast bacilli. Roentgen examination of the chest disclosed no abnormalities. An intradermal test with tuberculin was positive. The Wasser-

mann and the Kahn reaction of the blood were negative. Urinalysis and a complete blood count gave normal results. The results of culture and inoculation of guinea-pigs have not yet been reported. Sections showed tuberculous architecture with formation of giant cells.

DISCUSSION

DR. F. D. WEIDMAN: The laboratory report is surprising. I think that most of the members would regard the condition as hidradenitis axillaris. The tremendous number of acid-fast organisms is a little out of the ordinary for tuberculosis. In the axilla, of course, the sweat and sebaceous glands are highly developed; with plenty of grease available there is a medium closely approaching the composition of butter, and it is known that there are other acid-fast organisms besides the tubercle bacillus, for example, the butter bacillus. I am glad to hear that inoculation of guinea-pigs has been attempted. The tuberculous architecture argues against the invasion with butter bacilli, and I dare say that there will be evidence indicating that the condition is really tuberculous.

A CASE FOR DIAGNOSIS. Presented by DR. S. S. GREENBAUM.

H. M., a Negro aged 46, presents numerous small, apparently follicular atrophic lesions of five months' duration scattered over the vertex of the scalp. A few inflammatory papules are also present. Many of the pitlike depressions show tufts of half a dozen or more hairs. The patient's chief complaint is itching.

DISCUSSION

DR. F. D. WEIDMAN: I suggest the diagnosis of suppurative folliculitis with atrophy, of the order, perhaps, of folliculitis decalvans. Of course, it will be necessary to determine whether yeast cells are present and whether this might be a case of furunculosis cryptococcica of Castellani.

DR. S. S. GREENBAUM: This patient came to the clinic this afternoon, and on close examination it was found that there are bundles of hairs coming out apparently at many points, simulating ichthyosis thysanotrichica. The spinous papules present in that condition may have been scratched out by the patient, exposing these atrophic areas. I am inclined to regard the condition as necrotic acne. The case is interesting because of the limitation of the dermatosis to the scalp.

DR. V. C. GARNER: I agree with the diagnosis of acne necrotica.

LICHEN PLANUS ATROPHICUS. Presented by DR. THOMAS BUTTERWORTH, Reading, Pa.

F. G., a woman aged 58, presents "white spots" of four months' duration on the shoulders, front of the chest and left buttock. In December 1934, one month before the first appearance of the eruption, a hemorrhoidectomy was performed with the patient under spinal anesthesia. An adenoma of the rectum was also removed at that time. Irregular polygonal flat-topped white papules and macules are distributed over the shoulders, presternum and left buttock. In places the lesions are grouped, forming plaques. In many instances the isolated papules present a slight depression on their surfaces. Histologic examination showed that at the present stage of development the lesion did not exhibit any features absolutely differential between atrophic lichen planus and morphea guttata. There was no lymphocytic infiltration in the section such as should be present in the earlier and characteristic stage of lichen planus. However, this infiltration disappears in old lesions. Against the diagnosis of morphea was the fact that there was no evidence of preexisting formation of fibrous tissue in the deeper parts of the corium. The thin atrophic epiderm seen in the sections is common to both of the dermatoses named. An extremely narrow zone of degenerate collagenous material appeared immediately below the epiderm. This could well represent the location of a preexistent zone of lymphocytic infiltration such as would be expected in lichen planus.

DISCUSSION

DR. W. O. ROOP, Atlantic City, N. J.: According to what the patient told me, she has had practically no subjective symptoms. If that is true, that fact together with the clinical picture appears indicative of morphea.

DR. V. C. GARNER: I suggest the diagnosis of dermatitis lichenoides chronica atrophicans of Csillag, the lichen albus of von Zumbusch. I think that the case is comparable to that described by Shelmire and Wise.

DR. F. D. WEIDMAN: I suggest the diagnosis of white-spot disease of Jadassohn. There is a definite infiltration in the patches. I remember Wise's report and lantern slides. As I recall, there were larger patches widespread over the body.

DR. S. S. GREENBAUM: The patient says that there has never been any itching. I cannot subscribe to the diagnosis of atrophic lichen planus. I agree with Dr. Weidman's diagnosis of white-spot disease or morphea guttata.

DR. V. C. GARNER: My understanding of white-spot disease is that there are three varieties: (1) lichen planus atrophicans et sclerosus of Hallopeau; (2) lichen albus of von Zumbusch, and (3) morphea guttata. Obviously the case must fit into one of the three categories, and in view of the negative results of the histologic examination it seems that the diagnosis of lichen planus of von Zumbusch is probably the correct one.

LUPUS ERYTHEMATOSUS WITH INVOLVEMENT OF THE CONJUNCTIVAE. Presented by DR. ROBERT L. GILMAN.

A. H., a woman aged 26, presents an erythematodiscoid eruption on the cheeks and nose; the conjunctivae are swollen, red and inflamed. The condition has been present for six months.

DISCUSSION

DR. J. V. KLAUDER: The patient presents lesions of the conjunctivae which in my opinion are typical of lupus erythematosus, namely, elevated velvety plaques similar to those present in the two cases of lupus erythematosus of the conjunctiva that Dr. De Long and I reported (*Arch. Ophth.* **7**:856 [June] 1932). The appearance of the conjunctivae of our patients corresponded to the descriptions in the few other case reports in the literature. The conjunctival and the facial lesions disappeared after administration of gold and sodium thiosulphate; hence I had no doubt as to their being lesions of lupus erythematosus. It is interesting to comment on the apparent rarity of this condition. In patients with lupus erythematosus I now examine the conjunctivae as a routine. In addition, the patient shown this evening presents typical lupus erythematosus on the eyelids—atrophy and loss of the cilia.

DR. J. M. SCHILDKRAUT, Trenton, N. J.: I had a similar case of lupus erythematosus involving the conjunctivae and eyelids that cleared up nicely under treatment with a gold preparation.

SARCOID. Presented by DR. J. V. KLAUDER.

A. S., a Negress aged 24, presents dark brown translucent lesions on the face, including the eyelids and lips, and on the neck and upper portion of the chest. Some lesions are the size of a pea, and some, that of a pinhead. The patient looks ill; she has lost weight and has a persistent cough. Grossly, the fingers are normal. The patient claims to have been in good health until November 1934, when she contracted a cold, which has persisted until now. There is active pulmonary tuberculosis.

DISCUSSION

DR. S. S. GREENBAUM: I know that patients with this type of condition have been presented from time to time before the society with a diagnosis of sarcoid, and rightly so in view of the present classification. I rather believe, however, that the disorder represents a true tuberculous infection of the skin. I know that the

case has not been studied thoroughly, but I believe that in cases of this type inoculation of guinea-pigs or other methods of study would show tubercle bacilli.

DR. F. D. WEIDMAN: That is what Dr. Klauder and I thought in the first case of this kind that we reported, but there were at least two examinations of the skin. Inoculation of guinea-pigs gave negative results, and a biopsy was made on material from the epitrochlear lymph nodes, which were even larger than in this patient, being the size of beans and perhaps larger. I am inclined to believe that the condition may be in one of the earlier stages; it will be necessary to await ulceration of these nodules such as took place in our cases in which ulcers developed. Have these lesions ever had horny scales?

DR. J. V. KLAUDER: I am not presenting the patient as having the type of tuberculosis of the skin that appears to be distinctive of the Negro as reported by Dr. Weidman and me (Multiple Sarcoid-Like Granulomas of the Skin of Undetermined Nature, ARCH. DERMAT. & SYPH. **12**:171 [Aug.] 1925; **13**:675 [May] 1926; *Dermat. Wchnschr.* **99**:118 [Dec.] 1934). I believe, however, that the eruption now shown will change into the type Dr. Weidman and I described.

DR. S. S. GREENBAUM: Several lesions on the side of the face are definitely undergoing ulceration.

DR. V. C. GARNER: The case illustrates the polymorphism of tuberculosis of the skin. I think in their miliary character, their pearly translucency and their distribution about the eyelids the lesions on the face closely resemble the condition known as lupus miliaris disseminatus faciei.

PERIFOLLICULITIS CAPITIS ABSCEDENS ET SUFFODIENS. Presented by DR. W. O. ROOP, Atlantic City, N. J.

E. R., a Negro aged 28, presents an eruption on the scalp which has persisted for eight months. He was treated for extensive pustular acne of the face about six years ago. Seven years ago he had a small penile lesion. The Wassermann reaction of the blood was 4 plus, and he is receiving antisyphilitic treatment. There are numerous pea-sized and larger granulomatous nodules studding the greater portion of the scalp; these nodules develop on undermined subcutaneous abscesses. On pressure pus exudes from the lesions. The surface of the scalp is somewhat furrowed as a result of the recurrent abscesses The areas between the granulomatous lesions are covered by small cicatrices, the sites of healed lesions The face shows extensive scarring as the result of an old pustular acne. The lesions on the scalp have not been influenced by the antisyphilitic treatment the patient is receiving. Biopsy of a nodule showed epithelial hyperplasia and hyperkeratosis. In the central core was a loose edematous reticulum which, in general, had the appearance of a subacute inflammatory process. There were numerous infiltrating leukocytes, much fibrinous exudate and a large number of newly formed capillaries engorged with blood. The tissue resembled granulation tissue, except that fibroblasts were not numerous. Hair and scrapings did not show fungi. The urine and the blood count were normal. The Wassermann and Kahn reactions of the blood were both 4 plus.

DISCUSSION

DR. F. D. WEIDMAN: This patient states that he has had pustules on the upper lip; at present the lip shows marked sycosiform scarring; there have also been pustules in the eyebrows, and there is at least one there now. The patient gave no definite information as to the occurrence of pustules in the axillae. My co-workers and I have recently seen a number of cases of extensive sycosis vulgaris which began in the nose, with involvement of the mustache region; in one there were acne-like pustules over the chest and tremendous abscesses in the axillae, and on looking up the subject in Jadassohn's "Handbuch" I found that the scalp also can become involved. It is not regularly involved, to be sure, but when the disease is widely disseminated the scalp may become affected. I think possibly this

patient presents one of those unusually widespread examples of sycosis vulgaris which has extended also to the scalp. Has there been involvement of the axillae at any time?

DR. W. O. ROOP, Atlantic City, N. J.: No, not while the patient has been under my observation. Personally, I think that he presents a typical picture of the condition described as perifolliculitis capitis. The striking features are these numerous granulomas that break down and form scars and their development on undermined abscesses; these features fit in exactly with what is observed in this condition. Few books on dermatology give a description of this disease. If the diagnosis is correct, the disease either is rare or is not properly recognized when it is seen. I have taken the time to look up the reports of the society proceedings for the last few years in the ARCHIVES, and I find that cases of this disease are reported not more than four times; two of these four cases, I believe, occurred in Negroes. Reference is made to associated acne of the face. The condition is exceedingly resistant to treatment.

DR. V. C. GARNER: The granulomatous character of the lesions and the absence of pus canalization suggested to my mind the diagnosis of endothelioma capitis of Kaposi.

SARCOIDOSIS (BOECK OR BESNIER-BOECK DISEASE). Presented by Dr. S. S. GREENBAUM.

CASE 1.—J. C. W., a man aged 23, says that four years ago he noticed progressive swelling of the entire index finger of the right hand. There was no associated tenderness, redness or limitation of movement. Sharp localized pain was present only on pressure. Three months later the little finger of the right hand became similarly involved, and subsequently the remaining digits of that hand also became affected. A year after the onset the thumb of the left hand showed a similar change, and later the condition was noted in the fingers. The swelling has never extended beyond the base of the affected fingers. The toes were never involved. Recently some of the fingers first involved have become stiff, and complete flexion is impossible. Strength is diminished in the fingers. There are multiple warts on the right hand, the forearms and the face. About three weeks ago the patient received roentgen treatment for these warts, and since then the right index finger has been more tender on movement and has become discolored. During the past three months the bridge of the nose has increased in size. There have been occasional nosebleeds, usually precipitated by picking or blowing the nose. There is a well circumscribed elevated reddish lesion on the right cheek. That lesion has been present for two months. Within the past two months there have appeared over the extensor surfaces of the arms several flat indurated erythematous intradermal plaques the size of a quarter. There is generalized adenopathy without adherence or tenderness; the spleen is palpable 3 fingerbreadths below the costal margin; the nasal septum is deviated to the left, and crusting is present. A hard, smooth swelling at the bridge of the nose, which somewhat obstructs breathing, is present. The fingers are thickened or swollen, particularly about the first phalangeal joint. Roentgen examination of the long bones showed no changes except small areas of rarefaction in the lower end of the radius and ulna. The sella turcica was normal. The hands showed areas of rarefaction with considerable deformity in bony contour. Roentgenograms of the chest showed no abnormalities. The feet showed early stages of changes similar to those present in the hands. All studies of the blood, including a complete cell count, chemical examination and fixation tests, gave normal results. The tuberculin test was negative. Bacteriologic examinations of the skin of the fingers gave negative results. A hemolytic streptococcus was grown from the left nasal chamber. Inoculation of guinea-pigs with tissue from a lymph gland gave negative results.

CASE 2.—K. G., a Negress aged 35, presents marked scarring of the left cornea and large pudgy hands. The ocular condition has recurred since child-

hood and has been regarded as being possibly due to congenital syphilis. Swelling of the hands was first noticed in 1915; it has persisted since then. On the right flank and left knee are two oval skin-colored plaques with slightly elevated, well defined borders and depressed, atrophic centers. The nails are thickened. Moderate adenopathy is present. General physical examination gave essentially negative results except for the fact that the liver was palpable. Roentgenograms of the pelvis, hip joints and knees showed no abnormalities. The hands show extensive atrophic and hypertrophic arthritis with marked alteration in the bony structure of the phalanges. The feet show similar changes. The following diagnoses based on the roentgen findings were suggested: sarcoid, leprosy and coccidioidal granuloma. A blood count showed hemoglobin, 35 per cent; red cells, 3,880,000; white cells, 7,500; polymorphonuclears, 49 per cent; lymphocytes, 45 per cent. The Wassermann and Kahn reactions were strongly positive. The basal metabolic rate was plus 4. A biopsy was made by a general pathologist, and the condition was diagnosed as tuberculosis. Smears did not show the organism of lepra or the tubercle bacillus.

DISCUSSION

DR. S. S. GREENBAUM: Last month two or three patients with sarcoid were presented before the society; two exhibited lesions like the one that this man has on the right cheek. I believe, with Kissmeyer, that the time will come when this type of condition will be considered a disease sui generis—I call it "sarcoidosis," meaning "sarcoid disease," to differentiate it from sarcoid of tuberculous, leprous or syphilitic origin. These two patients present the same phenomena in the phalanges of both hands and feet. It appears to be a cystic condition of a number of the phalanges in the hands which roentgen and histologic studies have shown to consist, not of cystic changes, but of granulomatous infiltration into the canals with destruction of portions of the medulla. Some of them have become so infiltrated that the fingers have taken on a spindle-shaped appearance as the process spreads into the subcutaneous structures. The other curious feature about the man is the Mikulicz syndrome, that is, a progressive enlargement of the parotid glands. Both patients present general adenopathy and either splenomegaly or hepatomegaly. Both had negative reactions to tuberculin; this may show an anergic state or may be a proof that the condition is not tuberculous. In case 1 inoculations of glandular material into guinea-pigs gave negative results. Certainly the lesions of these two appear altogether different from those of patients presented by Dr. Klauder and Dr. Weidman at previous meetings of this society, and it may be that the lesions of the patients presented last month, which were typical sarcoids, are cutaneous expressions of the disease. Syphilis, for example, can apparently produce cutaneous lesions and nothing else, and the same thing may occur in cases of sarcoidosis. This, at least, is my conception of the Boeck-Besnier type of sarcoid.

A CASE FOR DIAGNOSIS. Presented by DR. I. C. CHIPMAN, Wilmington, Del.

F., a man aged 45, presents destructive ulcerative scarring lesions over both shins and the patellar region. The lesions are erythematous and show a distinct yellowish cast. There is some telangiectasia. Each eye shows a healed corneal ulcer which does not impair vision. There is a healed cupped-out scar on the penis. Scarring from a surgical operation in the inguinal region is present. The patient states that a sore appeared on the penis in 1912 and lasted for two months. At that time an operation for the removal of some inguinal glands was performed. The lesions on the shins started after the patient suffered trauma to the shins in 1918. The ocular lesions started in 1920. In 1912 the patient was given an unknown amount of arsphenamine. The Wassermann reaction was negative on several occasions; the blood count was normal. The patient was treated with neoarsphenamine, bismuth, potassium iodide and a gold preparation at different times. At present the lesions show improvement.

DISCUSSION

DR. F. D. WEIDMAN: I cannot suggest a diagnosis. I think that this patient presents one of the most peculiar conditions shown here this evening. The yellow color and the location on the shins are suggestive of necrobiosis diabeticorum. In the cases I have seen there was no ulceration, certainly not the degree of ulceration indicated by the depressed scars this patient has. I understand that diabetes has been definitely ruled out by laboratory tests. The other diagnosis to be considered, in view of the linear distribution of these lesions and the presence of some linear channels (dark from the presence of venous blood), is some variant of a dermatitis due to stasis, but the yellow color does not fit into that picture. I think, therefore, that the study of this case will not be complete unless a determination of the cholesterol content of the blood is made. Patients with xanthomatous diseases usually show a hypercholesteremia, and their lesions generally take on a yellow color. In this case the color may be an accidental feature of ulcers due to stasis resulting from associated hypercholesteremia. Another thing to be considered is that in regard to necrobiosis diabeticorum, I think, the trend of opinion is that the necrobiotic changes are referable to arteriosclerosis, which is in turn due to diabetes. If that is the case, diabetes need not always be fundamental to the arteriosclerosis. An arteriosclerosis with or without a dermatitis due to stasis in the presence of hypercholesteremia would produce a combination of circumstances such as that present in cases of xanthoma diabeticorum but without the diabetic features—which is the case in this patient. The corneal opacities, too, could be part of an arteriosclerotic complex. It is known that these ocular changes occur in cases of hypercholesteremia. It may well be that the deposits on the corneas which puzzle the ophthalmologists are deposits of cholesterol. They have a translucent, shining appearance that is not comparable to the opacities induced by fibrosis. In short, I think that the question of arteriosclerosis, the matter of associated circulatory disturbances and the possibility of an associated hypercholesteremia should be studied. This patient's disorder may be a new symptom complex —a nondiabetic necrobiosis lipoidica.

DR. I. C. CHIPMAN: This patient has received every metal preparation that appeared indicated, and when he was taking potassium iodide a palpable mass as large as an orange developed in the ileocecal region, on the side on which the inguinal glands were removed several years ago. When administration of potassium iodide was discontinued for a few days or a week, the mass disappeared entirely. Several years ago I had a patient with lupus erythematosus of the face who had a similar mass in the abdomen and whose condition was diagnosed as Hodgkin's disease. The mass in the abdomen was removed, and the lupus erythematosus cleared up. The type of the lesions in the cornea was never ascertained by the ophthalmologist.

STRIAE ATROPHICAE AFTER LOSS OF WEIGHT. Presented by DR. S. S. GREENBAUM.

Sophie F. and Samuel F. are aged 14 and 16, respectively. The girl presents some striae cutis distensae on the inner aspect of the upper portion of the arms and on the breast and hips. The condition was noticed about three months ago, after the patient went on a diet and lost 18 pounds (8.2 Kg.). The boy has the same condition, but there is no history of loss of weight. He is receiving treatment for psoriasis. The girl weighs 167 pounds (75.8 Kg.); the blood pressure was found to be 114 systolic and 70 diastolic; the sugar content of the blood was 74 mg. per hundred cubic centimeters; the basal metabolic rate was —8. A test for dextrose tolerance made on April 5, 1935 showed the following values for sugar: during fasting, blood, 74 mg. per hundred cubic centimeters, and urine, 0; after one hour, blood, 87 mg., and urine 0; after two hours, blood, 108 mg., and urine, 0; after three hours, blood, 118 mg., and urine, 0.

DISCUSSION

DR. S. S. GREENBAUM: Striae atrophicae is not a rare phenomenon at all, but in the last article on the subject by Ebert the question was brought up as to whether

or not these striae are due in some instances, at least, to an endocrine disturbance. While in the majority of cases it is true that they appear after overstretching of skin, such as occurs in pregnant women or in persons who suddenly gain weight, this girl states that she lost 18 pounds in a few months and that subsequently these atrophic striae appeared. Some studies of the endocrine condition were made, but only one of them has been completed and that showed a fairly normal basal metabolic rate. The occurrence of these striae has been reported to follow prolonged illness, tuberculosis or typhoid; hence they are not always the result of an overstretching of the skin. They are not all striae distensae. There must be some other factor as well in the production of some of these linear atrophies.

DR. J. M. SCHILDKRAUT, Trenton, N. J.: The inner aspect of the arms is hardly a site for overstretching of the skin. I think that such striae occur fairly commonly along the abdomen and hips.

A CASE FOR DIAGNOSIS. Presented by DR. H. J. SMITH.

In A. L., a girl aged 6 years, bullae developed on the back of the neck two months ago. They were excoriated by scratching. Subsequently lesions have developed over the entire body. On admission the lesions were numerous, circinate and ringlike; they presented an erythematous, somewhat infiltrated plaque with a raised border and were surrounded by vesicles and blebs. Some of the lesions were impetiginous. For the last two days a 5 per cent solution of ammoniated mercury has been applied to the arms only. The blood count showed 49 per cent hemoglobin, 3,630,000 red cells and 11,650 white cells, with 58 per cent polymorphonuclears, 22 per cent small lymphocytes and 20 per cent eosinophils.

DISCUSSION

DR. H. J. SMITH: My co-workers and I made a diagnosis of dermatitis herpetiformis. We thought the case was unusual because of the many large bullae around the edges. The intense itching that is ordinarily seen in cases of dermatitis herpetiformis was not present, but absence of itching in dermatitis herpetiformis in children is not unusual. Despite local measures, new bullae are appearing in the cleaned-up areas.

DR. F. D. WEIDMAN: I agree with Dr. Smith's diagnosis. The lesions are so numerous in places that they have coalesced into patches with sharp margination. One form of the bullous diseases known in the older literature as pemphigus circinatus was for quite a long while a particularly popular concept among the German dermatologists, who opposed the idea (favored by the French) that dermatitis herpetiformis was an entity. The Germans still contend that Duhring's disease is nothing more or less than pemphigus circinatus. All the members will recall the discussion about the therapeutic use of chromium sulphate at the Dermatological Conference of the Mississippi Valley. I do not think the last word has been said about this drug. My co-workers and I have tried it in two cases and have obtained good results in the early periods of administration, at least.

DR. V. C. GARNER: The impetiginous character of the lesions and their circinate arrangement made me wonder whether the case could not be classed as one of impetigo herpetiformis, a condition which, of course, is more common in pregnant women than in other patients but has been said to occur in male patients and at all ages.

DR. S. S. GREENBAUM: I agree with Dr. Smith. This case is one of juvenile dermatitis herpetiformis or hydroa puerorum of Unna.

LUPUS ERYTHEMATOSUS DISSEMINATUS. Presented by DR. S. S. GREENBAUM.

J. M., a woman aged 32, says that about two years ago she had a "bad tooth" extracted. The following day her left ear became red, swollen and painful. Soon there developed a papulopustular dermatitis of the face, which was followed by

the generalized dermatitis existing at present. Alopecia occurred simultaneously with the onset of the disorder. The patient is poorly nourished and looks ill. Nearly all the hair has fallen from the scalp and eyebrows. The eruption consists of erythematous macules with scaling, some of the older lesions showing areas of atrophy. The lungs, abdomen and heart were found essentially normal. The blood pressure was 140 systolic and 80 diastolic; the heart rate was rapid. A blood count made on Feb. 7, 1935, showed 39 per cent hemoglobin, 2,760,000 red cells and 3,900 white cells. On April 9 the hemoglobin was 55 per cent; there were 3,410,000 red cells, 5,000 white cells and 179,000 platelets. The Wassermann test was negative. The basal metabolic rate was + 30. All urinalyses gave essentially normal results.

DISCUSSION

DR. F. D. WEIDMAN: This patient has been presented at previous meetings. Her case is peculiar. She had one foot in the grave, and I expected that an autopsy would shed light on her condition. She was psychopathic and evidently had a severe constitutional disorder with cutaneous manifestations. An attempt was made to obtain information as to the internal aspects of the disease, but no foci of infection could be found. The treatment, whether because of the bismuth, the blood transfusions or Providence, has resulted in a spectacular recovery.

VAUGHN C. GARNER, M.D., *Secretary*

May 17, 1935

ROBERT L. GILMAN, M.D., *Chairman*

EPIDERMOLYSIS BULLOSA IN BROTHER AND SISTER. Presented by DR. JOHN B. LUDY.

G. C., a girl aged 9 years, and her brother, aged 11, present extensive scars and crusted areas over the exposed and prominent parts of the body: the knuckles, wrists, elbows and knees. The fingers and toes, owing to contracture, are "claw-like" in appearance, and the nails are missing. The tongue, the mucous membrane of the mouth and the cornea show signs of involvement. The eruption is always worse during the winter. Tests on the girl showed that the total urinary excretion of creatinine was 6.2 Gm. in twenty-four hours. The blood count was normal. The phosphate content of the blood was 1.8 mg. per hundred cubic centimeters; the creatinine content, 1.5 mg.; the calcium content, 10 mg. Tests on the boy showed that the total urinary excretion of creatinine was 8.7 Gm. The blood cell count was normal; the phosphate content of the blood, 2.4 mg. per hundred cubic centimeters; the creatinine content, 1.3 mg., and the calcium content, 6 mg.

DISCUSSION

DR. JOHN B. LUDY: In my opinion the chief point of interest in these cases is the creatinine content of the urine. The excretion in one case was 8.7 Gm., and in the other, 6.2 Gm., and I understand that the normal excretion of an adult is 0.6 Gm. The creatinine content of the blood was normal. Patients with this condition often feel better in winter than in summer. I should like to know whether the observation of an increased urinary creatinine content has been made before in cases of this kind.

DR. JOHN H. STOKES: I have never heard of its being made. I was interested to see a brother and sister with this rare condition.

PURPURA ANNULARIS TELANGIECTODES. Presented by DR. JOHN B. LUDY.

M. W., a man aged 45, says that five years ago lesions developed over the anterior surface of the legs. The eruption has spread by the addition of new

lesions and by peripheral extension. At present the lower portion of the legs shows the appearance characteristic of purpura annularis telangiectodes, namely, purplish macules, larger annular lesions with atrophic telangectatic centers and residual pigment. The biopsy specimen revealed perivascular lymphocytic infiltration, microscopic hemorrhagic foci and, possibly, endarteritis.

DISCUSSION

DR. FRANK C. KNOWLES: I saw the patient whose case Dr. MacKee reported (*J. Cutan. Dis.* **33**:129, 186 and 280, 1915), and I think that the condition of Dr. Ludy's patient almost exactly duplicates that described in the original report.

ACRODERMATITIS CHRONICA ATROPHICANS (SCHWENINGER-BUZZI ATROPHY). Presented by DR. JOHN B. LUDY.

E. L., a woman aged 33, for twenty years has had thinning, lividity and crinkling of the skin and prominent vessels on the right forearm and on the outer surface of the upper part of the right arm, along with a few spots of macular atrophy in which the round contours and lack of resistance to pressure (buttonholing) suggested the Schweninger-Buzzi type of atrophy. Laboratory tests showed: cholesterol, 220 mg. per hundred cubic centimeters of blood; creatinine, 1.3 mg., and calcium, 10.5 mg.

ACRODERMATITIS CHRONICA ATROPHICANS. Presented by DR. J. B. LUDY.

M. S., a woman aged 40, presents a classic acrodermatitis of eight years' duration involving both legs and the right thigh. When the patient was 6 years of age trauma to the legs resulted in fracture and extensive lacerations. Within the past two years a dollar-sized ulcer has developed over the right tendo Achillis. The blood count was normal; the blood calcium was 14 mg. per hundred cubic centimeters.

DISCUSSION

DR. JOHN B. LUDY: The grandmother of the first patient had the same condition, and the patient comes from within a few miles of Alsace, where I understand there are many cases of this condition. The other patient is also German and comes from within about 10 or 12 miles of Alsace.

ACANTHOSIS NIGRICANS. Presented by DR. JOHN B. LUDY.

V. R., a woman aged 20, says that when she was 6 years of age a black discoloration of the skin developed in the region of the forehead, around the mouth and over the back of the neck. Her parents dated the onset from the time of an accident in which she was supposed to have applied motor oil and gasoline to her face and neck and to have gone out in the sun to play. After exposure to the sun a severe and prolonged sunburn developed, and the skin never resumed a normal appearance. At present there is pigmentation over the entire torso, with thickening of the skin of the axillae and neck.

DISCUSSION

DR. D. M. SIDLICK: This patient presents a phase which is not commonly observed, namely, the juvenile type of acanthosis nigricans changing into the adult type.

DR. JOHN B. LUDY: This patient is now pregnant, and she had a child several years ago. She tells me that during the latter part of her pregnancy she feels better. I think the skin is better now than it was ten years ago.

ERYTHRODERMIE PITYRIASIQUE EN PLAQUE DISSEMINÉE (BROCQ). Presented by DR. JOHN B. LUDY.

C. N., a woman aged 33, presents lesions on the lower extremities These lesions are of five years' duration and began as a single spot on the tibial region;

later the eruption was augmented by the appearance of other lesions on the same and on the other side. Only the lower portions of the legs are affected, presenting roughly symmetrical areas which tend to be sharply defined; the eruption consists of atrophic patches with reddish-brown, telangiectatic, scarlike centers with no elevation above the normal skin. The Wassermann test was negative. No biopsy has been made. The sugar content of the blood was 85 mg. per hundred cubic centimeters.

DISCUSSION

Dr. Donald M. Pillsbury: I suggest the diagnosis of necrobiosis lipoidica diabeticorum.

Dr. S. S. Greenbaum: I object to the diagnosis, and I suggest the elimination of the condition named by Dr. Pillsbury, as well as of scleroderma, tuberculosis and syphilis. A biopsy should be made.

Dr. Frank C. Knowles: I believe that this is a case of morphea.

Dr. Vaughn C. Garner: It seems to me that the condition is entirely comparable to that of a woman presented at the Atlantic Dermatologic Conference in New York in the fall of 1934. That patient had similar lesions, which nearly all the members accepted as lesions of necrobiosis clinically but which pathologically showed the picture of morphea. I think that this patient has morphea, with changes in the elastica producing the yellowish discoloration.

Dr. John B. Ludy: I am willing to accept the diagnosis of morphea.

Pernio and Bazin's Disease. Presented by Dr. John B. Ludy.

F. Z., a girl aged 15, presents a localized erythema limited to the hands and lower portions of the legs. The skin of these areas is uniformly bluish red and moist. The areas on the legs become greatly indurated during the winter, suggesting Bazin's disease. The condition started two years ago, owing, so the mother believed, to exposure to cold without customary protection. It is present throughout the year but is much worse during the winter. The pulse rate is 72. Laboratory tests showed that the basal metabolic rate was + 4; the blood count was normal; the calcium content of the blood was 11.5 mg. per hundred cubic centimeters. Roentgen examination showed probable tuberculosis of the hilus.

DISCUSSION

Dr. S. S. Greenbaum: There is no evidence of Bazin's disease at the present time, nor is there, I believe, erythema pernio. I think that the patient has a fairly common condition, namely, acro-asphyxia or acrocyanosis, a chronic congestion which becomes worse during the winter and in cold weather, and a type of lesion which is good ground for the development of tuberculous lesions. I think that the patient should be examined for evidence of endocrine disturbances.

Dr. John H. Stokes: Adamson reported a series of these cases and pointed out the close relationship between these acrocyanotic and livedo-like changes and the tuberculids. He described and, I think, gave illustrations of an intermediate or link type, in which the retiform tissue was the site of the tuberculid. I think that this patient's disorder belongs in the general group of tuberculosis with a vascular background and should be studied from that angle.

Scleroderma. Presented by Dr. John B. Ludy.

J. A., a woman aged 25, shows a slight scaliness and inelasticity of the skin and diffuse pigmentation on the sides of the chest and neck. The skin is tight and leathery practically everywhere except on the toes. Sclerodactylia is present and impedes fine movements of the fingers. The patient claims that she was in perfect health until three years ago except that she always had a dry skin. Then she noticed that she was getting rather weak and lacked her usual energy, but she continued to work. Two years ago she noticed stiffness in the joints, and the skin

became glossy and tense. During the past year the skin of the face has grown tight, especially over the bridge of the nose. The patient is frail in appearance. The pupils react equally to light and in accommodation. The thyroid seems enlarged. Laboratory tests showed a marked increase in length of the metacarpal bones of both hands. The basal metabolic rate was + 4. Examination of the blood revealed evidence of a moderate secondary anemia. Chemical examination of the blood showed: urea, 26.7 mg. per hundred cubic centimeters; urea nitrogen, 12.7 mg.; phosphorus, 3.92 mg.; cholesterol, 200 mg.; calcium, 11.8 mg.; uric acid, 2.13 mg., and calcium, 17.8 mg. The patient was given typhoid vaccine intravenously and intramuscularly without result. A lumbar sympathetic ganglionectomy was performed in January 1935, and temporary improvement resulted.

DISCUSSION

DR. JOHN B. LUDY: This patient underwent a lumbar sympathectomy some months ago and was greatly improved for quite a while. I think she is better now than she was, but the vegetative nervous system, I understand, builds itself up quite promptly, and the symptoms will probably become as severe as they were before admission. The result of the sympathectomy is the only reason for presenting the patient.

DR. JOHN H. STOKES: Parathyroidectomy might be tried in cases of this sort, or the patient might be put on a calcium-elimination diet. The calcium content of the blood is high. The patient might be given ammonium chloride and an acidosis-producing diet. Pautrier recommends this. It was rather interesting to learn that the patient showed the Sellei type of acrodactylia and sclerodactylia, which brings up some interesting points of differentiation.

DR. DONALD M. PILLSBURY: In this case the use of pancreatic extracts as advised by Sellei might be of benefit.

DR. S. S. GREENBAUM: Has any one used ammonium chloride and obtained good results with it? The reason I ask is that I have used it in two cases of morphea, and in both of them the condition cleared up, leaving only pigmented spots.

DR. ABRAM STRAUSS: I should be interested to hear the end-results in the case so far as sympathectomy is concerned because in a case in which sympathectomy was performed there was a great deal of improvement at the time, but later a relapse occurred, and several months after the sympathectomy the condition became worse than ever.

DR. JOHN H. STOKES: I agree with Dr. Strauss on that point. I have seen cases of this kind in which sympathectomy left the patient worse than he was before the operation was performed. The benefit is usually only temporary.

DR. DONALD M. PILLSBURY: I believe that that has been the experience at the Mayo Clinic, where sympathectomy has been widely used. Initial improvement was noted, but it was not maintained.

CUTANEOUS NEUROMA. Presented by DR. JOHN B. LUDY.

M. J., a Negress aged 42, presents on each extremity from fifteen to twenty discrete firm, flattened, deeply pigmented tubercles, which vary in size from that of a split pea to that of a hazelnut. They are firmly incorporated in the skin, diffusely distributed, and do not follow the course of any nerve trunk. The lesions first appeared ten years ago, and new lesions appear gradually. Except for occasional periods of mild itching, they are symptomless. When the patient was between 18 and 25 years old she was troubled with prolonged "colds." She gained weight after that and considered herself well until the present lesions appeared. Roentgen examination of the chest showed cottony infiltration of the left apex suggestive of an old inflammatory condition, probably tuberculous. There were dense opaque shadows in the lower portion of the right side of the thorax and the costophrenic angle was obscured, the appearance being suggestive of a thickened pleura with

fluid. The Pirquet test was positive. The Wassermann test and an examination of the spinal fluid gave negative results. The patient has been on a salt-free diet for the last five years. Some lesions have disappeared; others are involuting.

DISCUSSION

DR. JOHN B. LUDY: The interesting phase of this case is that many of these nodules are involuting. When the case was reported (Ludy: Cutaneous Neuroma, ARCH. DERMAT. & SYPH. **21**:419 [March] 1930) the patient had active tuberculosis; she was underweight, and now the roentgenograms show no signs of any active lesions at all and apparently there is much improvement.

DR. S. S. GREENBAUM: Is it not unusual for neuromatous nodules not to show tenderness?

DR. JOHN B. LUDY: I think there should be tenderness, but this patient has paroxysmal attacks of intense itching during which she complains of a great deal of pain and tenderness.

DR. JOHN H. STOKES: I wish to suggest some alternative possibilities. As is well known, in Negro patients keloidal changes rather easily follow slight trauma with infection, and a prurigo nodularis can present some rather astonishing problems in these patients. Another possibility, of which I saw an illustration during my association with the Mayo Clinic, is that there may be a type of tuberculosis which gives rise to these extraordinary keloidal-looking nodules, the initial lesion being a pseudofuruncle closely resembling a violent reaction to tuberculin which, as it subsides, is followed by this keloidal change which produces the symmetrically distributed nodules over the extremities. The process seems to be confined to the extremities. I have in my collection a lantern slide showing the first eruption of that type which I saw. If I remember correctly, it occurred on the skin of a woman with tuberculosis. Dr. Ludy's patient has had tuberculosis, and therefore that should be considered as a possible diagnosis.

DR. FRANK C. KNOWLES: Is there any itching?

DR. JOHN B. LUDY: Occasionally.

DR. FRANK C. KNOWLES: The eruption looks like a prurigo nodularis.

MULTIPLE BENIGN TUMOR-LIKE NEW GROWTHS OF THE SKIN (SCHWENINGER-BUZZI TYPE). LUPUS ERYTHEMATOSUS. Presented by DR. LOUIS GOLDSTEIN.

B. W., a woman aged 24, presents skin-colored lesions which she first noticed on the back about a year ago. They gradually progressed, involving the shoulders, chest and entire upper part of the back. Some of the lesions present discrete elevations of a soft consistency; others are distinctly bladder-like. The older lesions, especially those which are about to regress, present a shriveled appearance. Many pigmented macules suggestive of scars are also present. Areas of fine telangiectasia are present over some lesions. The patient also presents on the face a few circumscribed slightly elevated reddish macules covered with adherent grayish scales. There are no subjective symptoms. The urinalysis, blood count, differential count and chemical examination of the blood gave normal results. The Wassermann reaction of the blood was negative. Microscopic examination showed moderate atrophy and ulceration of the epithelium and in some places a slight acanthosis with localized intra-epidermal areas of degeneration. The underlying tissue showed fibrosis, moderate congestion, edema, lymphocytic infiltration and hyaline changes of the collagen bundles.

DISCUSSION

DR. S. S. GREENBAUM: The patient has macular atrophy, but I do not know whether to class it in any particular group. The feature that appears interesting to me is the occurrence of one or two atrophic lesions on the face and of the inflammatory lesions on the forehead and nose. The beginning of the atrophy is particularly on the patient's back. I saw a case of this type several months ago

in which apparently atrophy had developed, and yet several months later there was complete disappearance of any evidences of the disease.

DR. JOHN H. STOKES: I wish to call attention to the lesions on the scalp. There are completely denuded patches which, I think, are the only support for a diagnosis of lupus erythematosus. As far as classifying the condition as belonging to the Schweninger-Buzzi type is concerned, I am not an authority on the recognition of that syndrome nor have I seen the sections in this case, but I can say that in the first case occurring in America, which Pusey and Fred Harris recognized in Chicago and subsequently described, the picture was not in the least like that presented by this patient. Perhaps the conception has widened, or that case may have represented only a particular phase, but it was an unforgettable experience to poke one's finger into the hole of a tumor of the Schweninger-Buzzi type, to press on that little superficial, blister-like piece of skin and find one's finger going right through. One never forgets the experience; but I do not believe that the same condition is satisfactorily duplicated in this case.

DR. FRANK C. KNOWLES: I think these lesions represent a macular atrophy, and the summits of the lesions look much like the forerunner of the pitlike stage, which will come later. .

DR. ROBERT L. GILMAN: I agree with Dr. Knowles. I have seen only two or three cases which conform to Dr. Stokes' description. I understand that the eruption on the back is of only a year's duration.

DR. THOMAS BUTTERWORTH, Reading, Pa.: I believe there is too much inflammatory reaction in this case for the lesions to be tumors of the Schweninger-Buzzi type. Some of them are definitely infiltrated, and the histologic report states that there is a lymphocyte infiltration in the involved areas besides other signs of inflammation which do not occur in the multiple benign tumor-like new growths of the Schweninger-Buzzi type.

DR. LOUIS GOLDSTEIN: The inflammatory appearance is caused by the fact that so many examiners have handled the lesions. The lesions did not present any inflammation before they were examined.

A CASE FOR DIAGNOSIS. Presented by DR. V. C. GARNER.

C. H., a girl aged 15, presents sharply marginated hyperkeratosis of the entire palms and soles. Small hyperkeratotic areas have recently developed on the dorsa of the feet; ill defined follicular papular lesions have appeared over the anterior aspects of the knees, and hyperkeratotic plaques are present over the extensor surfaces of the elbows and over the sacral region. The backs of the fingers are not involved. The onset, which occurred in February 1935, was sudden. Scrapings from the feet examined with potassium hydroxide showed no fungi. There has been little or no response to 2 skin units of roentgen radiation (fractional doses of ¼ unit skin dose), crude coal tar, 10 per cent solution of salicylic acid and other measures.

DISCUSSION

DR. W. O. ROOP, Atlantic City, N. J.: If mycotic infections can be positively ruled out, I think that the diagnosis of psoriasis can reasonably be considered. There is some involvement of both knees, particularly the right, and I have seen patients with typical lesions of psoriasis on the trunk who presented lesions on the palms and soles identical with those of this patient.

DR. JOHN H. STOKES: I am sure that nearly all the members will recall at least one example of this acute palmar and plantar condition with tremendous keratotic development occurring in young persons; it may be mycotic, though fungi cannot be demonstrated. Dr. Garner kindly pointed out to me some things that I should have missed in an ordinary inspection, among others, the grouped follicular eruption over the vertebrae in the lumbar region, which suggests a follicular dermatophytid or a beginning pityriasis rubra pilaris, though I have never seen the latter condition begin in this way. In studying one case, that of a young

child, I looked up the literature and found that there was a recognized acute type of palmar and plantar hyperkeratosis; at this time the condition is probably included in the growing conception of dermatophytosis. But it is still sub judice what is the matter with this patient. I do not think I ought to pass by this interesting case without saying that I neglected to ask whether the patient had been taking arsenic. In persons who are susceptible to the drug acute eruptions on the palms and soles have followed the taking of even small doses of arsenic.

DR. VAUGHN C. GARNER: There is no history of ingestion of drugs, except that a week ago I prescribed arsenic in the form of pills. I have considered the possibility of this disorder being one of the acquired types of keratoderma palmare et plantare. There are such cases on record, and clinically the lesions conform to the picture of that condition.

LUPUS VULGARIS. Presented by DR. THOMAS BUTTERWORTH, Reading, Pa.

C. J. B., a woman aged 21, presented on April 1, 1935, a smooth, flat, scaly reddish-brown patch on the right side of the neck, with typical apple jelly nodules in the borders. The center of the patch showed a tendency toward atrophy. The patient said that when she was 2 years old the lymph glands of the right side of the neck had shown enlargement. The swelling was incised by a surgeon, and healing was uneventful, but the present lesion appeared shortly after. At present, in the site originally occupied by the diseased gland there is a flat red scar. The entire surface is smooth with the exception of a small region in the lower part which has a slight keloidal tendency. The patient has been treated unsatisfactorily with ultraviolet and roentgen irradiation, intravenous injections of a gold preparation and a Gerson diet. The entire lesion was destroyed by electrocoagulation on April 1, 1935, and finely pulverized potassium permanganate was applied to the site.

LUPUS SERPIGINOSUS WITH ELEPHANTIASIS. Presented by DR. THOMAS BUTTERWORTH, Reading, Pa.

G. N., a woman aged 24, says that in the spring of 1927, when she was 16, an ulcer the size of a quarter developed on the left leg. This was followed in rapid succession by the development of other sores on the leg and a gradual enlargement of the entire extremity. When the patient was first seen, on Nov. 22, 1934, the left leg was greatly enlarged in its entirety, but the excess growth was particularly marked about the ankle. On all aspects of the thigh and about the knees were numerous serpiginous, gyrate and annular crusted warty thickenings. In places there were small ragged, dirty, foul-smelling ulcerations covered with abundant crusting. On the outer aspect of the leg there was a deep pus-discharging C-shaped ulcer. The lesions have had a tendency toward peripheral extension with the formation of central atrophy. Recurrences have taken place within the scar in several places. The swelling of the leg was firm and did not pit on pressure. On three occasions, under gas anesthesia, the lesions on the leg and on the inner and outer sides of the thigh were successively destroyed by curettage and electrocoagulation, which was followed by the application of finely pulverized potassium permanganate. Healing was slow but uneventful, but a small ulcerative area on the outer side of the leg did not heal and will probably need further coagulation. At present some of the scars are perfectly flat, while others, particularly those about the knees, are keloidal. Medical and gynecological examinations gave negative results. The Mantoux test showed a wheal measuring 1 cm. as an immediate reaction. In forty-eight hours a 1 cm. area of papules and a 2.5 cm. area of erythema developed. Smears for blastomycetes were negative. The Wassermann and Kahn reactions were negative. Roentgen examinations of the bones of both legs and of the chest showed no abnormalities. The report on a biopsy, as received from the Vanderbilt Clinic on Aug. 15, 1935, was tuberculosis of the leg. That diagnosis was later confirmed at the Reading Hospital.

DISCUSSION

DR. FRANK C. KNOWLES: I think that Dr. Butterworth is to be congratulated on his success in cases of lupus vulgaris and on the patience with which he has carried out the treatment. I think that in the case of serpiginous eruption of lupus vulgaris the result is magnificent. In regard to the case of erythematous lupus of the neck in which the same line of treatment has been followed, I wonder whether in certain instances it might not prove rather dangerous to try a desiccation after roentgen irradiation has been used. I wonder whether telangiectasia might not develop as a result of destructive measures following a certain amount of roentgen irradiation.

DR. JOHN H. STOKES: I should like to remark on the fine character of the work that has been done in both these cases by Dr. Butterworth and to emphasize the fact that surgical intervention certainly seems to be the proper treatment in cases of cutaneous tuberculosis of this type. Scarcely any one in this country, at least, who surveys the literature, would be likely to yield to the tendency to use roentgen irradiation in cases of cutaneous tuberculosis. The use of that method is passing rapidly to the Continent. A number of die-hards who have the equipment will continue to use roentgen irradiation for a long time, but surgical intervention and administration of tuberculin are coming more and more to the front.

DR. FRANK C. KNOWLES: I think that a salt-free diet should be tried in extensive cases of tuberculosis of the skin.

DR. THOMAS BUTTERWORTH, Reading, Pa.: The patient is following such a diet now.

DR. S. S. GREENBAUM: I also want to congratulate Dr. Butterworth. But I want to call attention to the lesion presented by this patient. I think it represents tuberculous lymphangitis in addition to the lupus. The treatment for cutaneous tuberculosis is to do exactly what nature does in cases of pulmonary tuberculosis, namely, heal it by fibrosis. Even when healing takes place with scar formation, nodules may develop not only in the scar but, in cases in which tissue has been replaced by plastic surgery, in the new tissue.

Book Reviews

The Brain as an Organ: Its Postmortem Study and Interpretation. By Frederic Wertham, M.D., and Florence Wertham. With an introduction by Adolf Meyer, M.D. Price, $7.50. Pp. 538, with 166 plates. New York: The Macmillan Company, 1934.

The simple manner of presentation makes the most modern findings in this difficult field accessible for the first time to physicians at large and thus enables the dermatologist and syphilologist to obtain accurate information on questions which have heretofore been the esoteric property of the nueropathologist.

The authors point out that studies on the pathology and histopathology of the brain have been hampered by several important obstacles. The first is that neuropathologists have successfully compiled a mass of data concerning neurologic changes, but have failed to coordinate them with the findings in the other parts of the affected body; the second is that changes in the central nervous system have frequently been recorded and regarded as pathognomonic without a sufficient number of normal controls, and the third is the subjective approach of the investigator who, overawed by the importance of the tissue he was studying, was inclined to study it as a thing apart, different from all the other organs of the body and not amenable to the same methods of interpretation or to be regarded as subject to the same fundamental laws. The title signifies that the authors have from the outset determined to avoid the errors which must ensue if the brain is regarded as anything more or anything else than an organ. This new presentation will appeal to the dermatologist, for it fits in with newer dermatologic concepts (see, for instance, page 2). The point of view expressed is reminiscent of the dermatologic recognition that even typical morphe do not represent etiologic entities, that, for instance, not all tubercles mean tuberculosis; in other words, morphe are but reaction forms to a large variety of noxae.

Of special interest to the dermatologist should be the descriptions of histologic technic which have been capable of bringing to light changes in a sister ectodermal tissue. Many of these technics have not yet been tried on the skin and would seem worthy of attempting. Syphilologists will be interested in this first published description of the new gold-silver method of Jahnel for the staining of spirochetes in frozen sections. The description and classification of the changes in paresis and cerebrospinal syphilis are presented in a complete, logical and precise form. The new dynamic classification employed brings to light clearly for the first time the logical relationships between such diseases as tuberous sclerosis, Recklinghausen's disease, syringomyelia and the concomitant skin diseases of the two former conditions. It is to be regretted that the authors have failed to mention the *vascular dermatologic* disorders sometimes accompanying the *vascular cerebral* disorders in epilepsy and have not called attention to the fact that the brain structures can act as the shock tissue in various forms of hypersensitivity of other organs, as is the case, for instance, in various drug idiosyncrasies, e. g., those due to bromides and those due to arsphenamine. The plates are both instructive and beautiful. There is a full index of twenty-nine pages.

Books Received

THÉRAPEUTIQUE DE LA PARALYSIE GÉNÉRALE. Marcel Pinard, Albert Fiehrer and Marcel Tavennec. Price, 22 francs. Pp. 120. Paris: Gaston Doin & Cie, 1934.

NOUVELLES LETTRES À UN MÉDECIN PRATICIEN SUR LA DERMATOLOGIE ET LA VÉNÉRÉOLOGIE. Dr. Clément Simon. Price, 35 francs. Pp. 226. Paris: Masson et Cie, 1935.

Directory of Dermatologic Societies *

INTERNATIONAL

NINTH INTERNATIONAL CONGRESS OF DERMATOLOGY AND SYPHILOLOGY

American Secretary: Dr. Howard Fox, 140 E. 54th St., New York.

FOREIGN

BRITISH ASSOCIATION OF DERMATOLOGY AND SYPHILOLOGY
(CANADIAN BRANCH)

H. A. Dixon, President, Medical Arts Bldg., Toronto, Ont.
Norman Wrong, Secretary-Treasurer, Medical Arts Bldg., Toronto, Ont.
Place: Toronto, Ont. Time: May 1936.

ROYAL SOCIETY OF MEDICINE, SECTION OF DERMATOLOGY

Henry MacCormac, President, 23, Wimpole St., London, W. 1.
R. T. Brain, Secretary, 132, Harley St., London, W. 1.

NATIONAL DERMATOLOGIC SOCIETIES

AMERICAN MEDICAL ASSOCIATION, SCIENTIFIC ASSEMBLY, SECTION ON DERMATOLOGY AND SYPHILOLOGY

Harry R. Foerster, Chairman, 208 E. Wisconsin Ave., Milwaukee.
J. Bedford Shelmire, Secretary, 1719 Pacific Ave., Dallas, Texas.
Place: Kansas City, Mo. Time: May 11-15, 1936.

AMERICAN BOARD OF DERMATOLOGY AND SYPHILOLOGY

Howard Fox, President, 140 E. 54th St., New York.
C. Guy Lane, Secretary, 416 Marlborough St., Boston.
Place: Kansas City, Mo. Time: May 11-12, 1936.

AMERICAN DERMATOLOGICAL ASSOCIATION

C. Guy Lane, President, 416 Marlboro St., Boston.
F. D. Weidman, Secretary, University of Pennsylvania, Philadelphia.
Place: New Ocean House, Swampscott, Mass. Time: June 4-6, 1936.

SECTIONAL DERMATOLOGIC SOCIETIES

CENTRAL STATES DERMATOLOGICAL ASSOCIATION

Samuel Goldblatt, President, 3208 Colerain Ave., Cincinnati.
Raymond G. Senour, Secretary-Treasurer, 19 W. 7th St., Cincinnati.
Place: Cincinnati. Time: 1935.

IOWA AND WESTERN ILLINOIS DERMATOLOGICAL ASSOCIATION

J. C. Kessler, President, University Hospital, Iowa City.
Robert E. Jameson, Secretary, 1014 First National Bank Bldg., Davenport, Iowa.

SOUTHERN MEDICAL ASSOCIATION, SECTION ON DERMATOLOGY AND SYPHILOLOGY

J. W. Roussel, Chairman, 150 Baronne St., New Orleans.
Cornelius F. Lehmann, Secretary, 705 E. Houston St., San Antonio, Texas.

* Secretaries of dermatologic societies are requested to furnish the information necessary for the editor to make this list complete and to keep it up to date.

STATE DERMATOLOGIC SOCIETIES

California Medical Association, Scientific Assembly, Dermatology and Syphilology Section

William H. Goeckerman, Chairman, 1680 N. Vine St., Hollywood.
Stanley O. Chambers, Secretary, 1210 Roosevelt Bldg., Los Angeles.

Florida Society of Dermatology and Syphilology

J. L. Kirby-Smith, Chairman, 204 Laura St, Jacksonville.
W. M. Sams, Secretary, 310 Ingram Bldg., Miami.

Louisiana Dermatological Society

M. T. Van Studdiford, President, 912 Pere Marquette Bldg., New Orleans.
R. A. Oriol, Secretary-Treasurer, Maison Blanche Bldg., New Orleans.

Massachusetts Medical Society, Section on Dermatology and Syphilology

Harvey P. Towle, President, 453 Marlborough St., Boston.
Rudolf Jacoby, Secretary, 270 Commonwealth Ave., Boston.

Medical Society of the State of New York, Section on Dermatology and Syphilology

Louis Tulipan, Chairman, 224 E. 17th St., New York.
C. H. Peachey, Secretary, 197 S. Goodman St., Rochester.

Medical Society of the State of Pennsylvania Section on Dermatology

Robert L. Gilman, Chairman, 1930 Chestnut St., Philadelphia.
Fred M. Jacob, Secretary, 7026 Jenkins Arcade Bldg., Pittsburgh.

Michigan State Medical Society, Section on Dermatology and Syphilology

A. R. Woodburne, Chairman, 26 Sheldon Ave., Grand Rapids.
G. Warren Hyde, Secretary, 2501 W. Grand Blvd., Detroit.

Minnesota Dermatological Society

Hamilton Montgomery, President, Mayo Clinic, Rochester.
D. D. Turnacliff, Secretary, 407 Medical Arts Bldg., Minneapolis.
Time: First Wednesday in October, December, February and April.

Oklahoma State Dermatological Society

Margne O. Nelson, President, 307 Medical Arts Bldg., Tulsa.
Harry Green, Secretary, 1116 Medical Arts Bldg., Tulsa.

Texas Dermatological Society

J. C. Michael, President, 1215 Walker Ave., Houston.
Everett R. Seale, Secretary, 1215 Walker Ave., Houston.
Place: Austin.

LOCAL DERMATOLOGIC SOCIETIES

Baltimore-Washington Dermatological Society

Dudley C. Smith, 30 University Pl., Charlottesville, Va.
Francis Ellis, Secretary, 104 W. Madison St., Baltimore.

Bronx Dermatological Society

Eugene F. Kelley, Chairman, 93 Radford St., Yonkers, N. Y.
Henry Silver, Secretary, 290 West End Ave., New York.

BROOKLYN DERMATOLOGICAL SOCIETY

Jacob Skeer, President, 272 E. 19th St., Brooklyn.
George F. Price, Secretary, 884 Lincoln Place, Brooklyn.
Time: Third Monday of each month except June, July, August and September.

BUFFALO-ROCHESTER DERMATOLOGICAL SOCIETY

Albert R. McFarland, President, 315 Alexander St., Rochester, N. Y.
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Max S. Wien, Secretary, 104 S. Michigan Ave., Chicago.

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H. G. Miskjian, President, 856 Rose Bldg., Cleveland.
E. W. Netherton, Secretary, 2020 E. 93d St., Cleveland.

DETROIT DERMATOLOGICAL SOCIETY

L. W. Shaffer, President, 1553 Woodward Ave, Detroit.
William G. Saunders, Secretary-Treasurer, 9203 Grand River Ave., Detroit.
Place: Cincinnati, Ohio. Joint meeting with Central States Dermatological Association. Time: November, 1935.

LOS ANGELES DERMATOLOGICAL SOCIETY

N. P. Anderson, Chairman, 2007 Wilshire Blvd., Los Angeles.
Thomas W. Nisbet, Secretary, 65 N. Madison Ave., Pasadena, Calif.
Time: Second Tuesday of each month, October to May, inclusive.

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Paul E. Bechet, Chairman, 55 Park Ave., New York.
Mihran B. Parounagian, Secretary, 126 E. 39th St., New York.

MONTREAL DERMATOLOGICAL SOCIETY

Alberic Marin, President, 1414 Drummond St., Montreal, Canada.
Paul Poirier, Secretary, 2073 St. Denis St., Montreal, Canada.

NEW ENGLAND DERMATOLOGICAL SOCIETY

William P. Boardman, President, 388 Marlborough St., Boston.
J. Harper Blaisdell, Secretary, 45 Bay State Road, Boston.

NEW YORK ACADEMY OF MEDICINE, SECTION OF DERMATOLOGY AND SYPHILIS

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Frank C. Combes, Secretary, 80 W. 40th St., New York.

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R. H. Rulison, Chairman, 145 E. 54th St., New York.
Eugene F. Traub, Secretary, 140 E. 54th St., New York.

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Charles McMartin, Chairman, 611 City National Bank Bldg., Omaha.
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Herbert J. Smith, Chairman, 3305 N. 17th St., Philadelphia.
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